



Clinical trial results:

A Phase 1/2 Dose-Escalation Study of Clofarabine in Combination With Etoposide and Cyclophosphamide in Pediatric Patients With Refractory or Relapsed Acute Leukemias

Summary

EudraCT number	2015-001174-18
Trial protocol	Outside EU/EEA
Global end of trial date	25 November 2009

Results information

Result version number	v1 (current)
This version publication date	23 May 2016
First version publication date	05 July 2015

Trial information

Trial identification

Sponsor protocol code	CLO21800205
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00315705
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Genzyme Corporation
Sponsor organisation address	500 Kendall Street, Cambridge, MA, United States, 02142
Public contact	Trial Transparency Team, Sanofi aventis recherche & développement, Contact- US@sanofi.com
Scientific contact	Trial Transparency Team, Sanofi aventis recherche & développement, Contact- US@sanofi.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	16 August 2010
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	25 November 2009
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective for the Phase I portion of the study is to determine the maximum tolerated dose (MTD), dose limiting toxicities (DLTs), and the recommended Phase II dose (RP2D) of clofarabine when used in combination with etoposide and cyclophosphamide and to assess the feasibility and safety of this combination regimen to treat children with refractory or relapsed acute lymphocytic leukemia (ALL) or acute myelogenous leukemia (AML).

Protection of trial subjects:

Paediatric subjects: The study was conducted by investigators experienced in the treatment of pediatric subjects. The parent(s) or guardian(s) as well as the children were fully informed of all pertinent aspects of the clinical trial as well as the possibility to discontinue at any time. In addition to the consent form for the parent(s)/guardian(s), an assent form in child appropriate language was provided and explained to the child. Repeated invasive procedures were minimized. The number of blood samples as well as the amount of blood drawn were adjusted according to age and weight. A topical anesthesia may have been used to minimize distress and discomfort.

Adult Subjects: Subjects were fully informed of all pertinent aspects of the clinical trial as well as the possibility to discontinue at any time in language and terms appropriate for the subject and considering the local culture. During the course of the trial, subjects were provided with individual subject cards indicating the nature of the trial the subject is participating, contact details and any information needed in the event of a medical emergency. Collected personal data and human biological samples were processed in compliance with the SanofiAventis Group Personal Data Protection Charter ensuring that the Group abides by the laws governing personal data protection in force in all countries in which it operates.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	11 March 2006
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 50
Worldwide total number of subjects	50
EEA total number of subjects	0

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	1
Children (2-11 years)	24
Adolescents (12-17 years)	19
Adults (18-64 years)	6
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

The study was conducted in two different phases. After determining the recommended Phase 2 dose in Phase 1 part, subjects were enrolled in Phase 2 part to estimate efficacy of clofarabine.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Phase 1: Clofarabine, Etoposide, Cyclophosphamide

Arm description:

Escalating dosage of the three drugs delivered.

Arm type	Experimental
Investigational medicinal product name	Clofarabine
Investigational medicinal product code	
Other name	Clolar, Evoltra
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

2040 mg/m²/day 2 hour intravenous (IV) infusion daily for 5 days of a 28 day cycle as the first of the three IV interventions administered. Maximum of 8 cycles was given.

Investigational medicinal product name	Etoposide
Investigational medicinal product code	
Other name	Eposin
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

75-100 mg/m²/day 2 hour intravenous (IV) infusion daily for 5 days of a 28 day cycle following clofarabine therapy. Maximum of 8 cycles was given.

Investigational medicinal product name	Cyclophosphamide
Investigational medicinal product code	
Other name	Endoxan, Revimmune, Cytosan
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

340440 mg/m²/day as 30-60 minute intravenous (IV) infusion daily for 5 days of a 28 day cycle following the other two interventions. Maximum of 8 cycles was given.

Arm title	Phase 2: Clofarabine, Etoposide, Cyclophosphamide
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Arm description:

The recommended phase 2 doses (RP2D) were delivered.

Arm type	Experimental
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Investigational medicinal product name	Clofarabine
Investigational medicinal product code	
Other name	Clolar, Evoltra
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

2040 mg/m²/day 2 hour intravenous (IV) infusion daily for 5 days of a 28 day cycle as the first of the three IV interventions administered. Maximum of 8 cycles was given.

Investigational medicinal product name	Etoposide
Investigational medicinal product code	
Other name	Eposin
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

75-100 mg/m²/day 2 hour intravenous (IV) infusion daily for 5 days of a 28 day cycle following clofarabine therapy. Maximum of 8 cycles was given.

Investigational medicinal product name	Cyclophosphamide
Investigational medicinal product code	
Other name	Endoxan, Revimmune, Cytosan
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

340440 mg/m²/day as 30-60 minute intravenous (IV) infusion daily for 5 days of a 28 day cycle following the other two interventions. Maximum of 8 cycles was given.

Number of subjects in period 1	Phase 1: Clofarabine, Etoposide, Cyclophosphamide	Phase 2: Clofarabine, Etoposide, Cyclophosphamide
Started	25	25
Completed	0	0
Not completed	25	25
Refused further treatment	1	-
Failure to achieve response	8	3
Physician Decision	-	4
Death	3	7
Disease relapse	4	1
Scheduled for transplant	9	8
Adverse event	-	1
Unspecified	-	1

Baseline characteristics

Reporting groups

Reporting group title	Phase 1: Clofarabine, Etoposide, Cyclophosphamide
Reporting group description: Escalating dosage of the three drugs delivered.	
Reporting group title	Phase 2: Clofarabine, Etoposide, Cyclophosphamide
Reporting group description: The recommended phase 2 doses (RP2D) were delivered.	

Reporting group values	Phase 1: Clofarabine, Etoposide, Cyclophosphamide	Phase 2: Clofarabine, Etoposide, Cyclophosphamide	Total
Number of subjects	25	25	50
Age categorical			
Units: Subjects			

Age continuous			
Units: years			
arithmetic mean	9.1	13.2	
standard deviation	± 5.03	± 5.25	-
Gender categorical			
Units: Subjects			
Female	10	9	19
Male	15	16	31
Ethnicity			
The two study phases were not designed to be reported in the aggregate.			
Units: Subjects			
Hispanic or Latino	5	10	15
Not Hispanic or Latino	20	15	35
Unknown or Not Reported	0	0	0
Race			
The two study phases were not designed to be reported in the aggregate.			
Units: Subjects			
American Indian or Alaska Native	0	1	1
Asian	3	2	5
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	4	2	6
White	16	12	28
More than one race	0	0	0
Unknown or Not Reported	2	8	10
Immunophenotype			
Applies to acute lymphoblastic leukemic (ALL) subjects only. Acute myelogenous leukemic (AML) subjects are not included. The two study phases were not designed to be reported in the aggregate.			
Units: Subjects			
B cell	13	21	34
T cell	5	1	6
Unknown	2	3	5

not included (AML subjects)	5	0	5
Count of Previous Anti-Leukemic (non-transplant) Treatment Regimens			
The two study phases were not designed to be reported in the aggregate.			
Units: Subjects			
1 regimen	4	4	8
2 regimens	18	14	32
3 regimens	3	7	10
Subjects with Previous Anti-Leukemic Transplant Regimens			
The two study phases were not designed to be reported in the aggregate.			
Units: Subjects			
Transplants	4	4	8
No transplants	21	21	42
Subjects Who Were Refractory to the Most Recent Previous Anti-Leukemic Treatment			
The answer "Yes" indicates the number of subjects who were refractory (unresponsive) to the most recent anti-leukemic treatment. The answer "No" represents subjects who were not refractory. The two study phases were not designed to be reported in the aggregate.			
Units: Subjects			
Yes	7	15	22
No	18	10	28
Subject Rating Using the Karnofsky/Lansky Performance Status Scale			
Baseline performance was rating using either the Karnofsky Performance Scale for subjects greater than 10 years old, or the Lansky Performance Scale for subjects 10 years or younger. Both scales range from 0-100 with 0 indicating dead or unresponsive and 100 indicating normal performance. The two study phases were not designed to be reported in the aggregate.			
Units: Subjects			
50	0	2	2
60	0	2	2
70	1	2	3
80	5	3	8
90	7	6	13
100	12	10	22
Percent Leukemic Blast Cells			
Percent of leukemic blast cells based on bone marrow aspirate. The two study phases were not designed to be reported in the aggregate.			
Units: percentage of total blast cells			
arithmetic mean	66.8	69.52	
standard deviation	± 24.85	± 23.56	-
Absolute Neutrophil Counts			
The two study phases were not designed to be reported in the aggregate.			
Units: 10 ⁹ /L			
arithmetic mean	1.93828	1.928	
standard deviation	± 3.049992	± 1.708126	-
White Blood Cell Counts			
The two study phases were not designed to be reported in the aggregate.			
Units: 10 ⁹ /L			
arithmetic mean	8.323	12.171	
standard deviation	± 9.1305	± 23.015	-

End points

End points reporting groups

Reporting group title	Phase 1: Clofarabine, Etoposide, Cyclophosphamide
Reporting group description: Escalating dosage of the three drugs delivered.	
Reporting group title	Phase 2: Clofarabine, Etoposide, Cyclophosphamide
Reporting group description: The recommended phase 2 doses (RP2D) were delivered.	
Subject analysis set title	Phase 1 - Cohort 1
Subject analysis set type	Full analysis
Subject analysis set description: Subjects were treated with clofarabine 20 mg/m ² , etoposide 75 mg/m ² , and cyclophosphamide 340 mg/m ² .	
Subject analysis set title	Phase 1 - Cohort 2
Subject analysis set type	Full analysis
Subject analysis set description: Subjects were treated with clofarabine 20 mg/m ² , etoposide 75 mg/m ² , and cyclophosphamide 440 mg/m ² .	
Subject analysis set title	Phase 1 - Cohort 3
Subject analysis set type	Full analysis
Subject analysis set description: Subjects were treated with clofarabine 20 mg/m ² , etoposide 100 mg/m ² , and cyclophosphamide 440 mg/m ² .	
Subject analysis set title	Phase 1 - Cohort 4
Subject analysis set type	Full analysis
Subject analysis set description: Subjects were treated with clofarabine 30 mg/m ² , etoposide 100 mg/m ² , and cyclophosphamide 440 mg/m ² .	
Subject analysis set title	Phase 1 - Cohort 5
Subject analysis set type	Full analysis
Subject analysis set description: Subjects were treated with clofarabine 40 mg/m ² , etoposide 100 mg/m ² , and cyclophosphamide 440 mg/m ² .	

Primary: Maximum Tolerated Dose (MTD) in Phase 1

End point title	Maximum Tolerated Dose (MTD) in Phase 1 ^[1]
End point description: The MTD was to be the highest dose level of clofarabine in combination with etoposide and cyclophosphamide that caused ≤ 1 of 6 subjects to experience a dose limiting toxicity (DLT) with the next higher dose level having at least 2 of 3 or 2 of 6 subjects experiencing a DLT. The MTD would be used as the recommended phase 2 dose (RP2D). If the MTD could not be determined, then the target dose of clofarabine 40 mg/m ² , etoposide 100 mg/m ² and cyclophosphamide 440 mg/m ² as taken by Cohort 5 was to become the RP2D. The rating scale used is 0 = not the MTD, 1 = the MTD. All phase 1 subjects.	
End point type	Primary
End point timeframe: Up to Day 42 (Phase 1 portion of study)	

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: As the analysis was descriptive, no statistical analysis is provided.

End point values	Phase 1 - Cohort 1	Phase 1 - Cohort 2	Phase 1 - Cohort 3	Phase 1 - Cohort 4
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	3	3	3	10
Units: units on a scale	0	0	0	0

End point values	Phase 1 - Cohort 5			
Subject group type	Subject analysis set			
Number of subjects analysed	6			
Units: units on a scale	0			

Statistical analyses

No statistical analyses for this end point

Primary: Subjects With Dose Limiting Toxicity in Phase 1

End point title	Subjects With Dose Limiting Toxicity in Phase 1 ^[2]
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End point description:

The number of subjects in each cohort that had dose limiting toxicity is summarized. Toxicities were reviewed by an independent Data Safety Monitoring Board (DSMB) who determined if additional subjects should be added to the cohort and the criteria for escalating to the next cohort. All phase 1 subjects

End point type	Primary
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End point timeframe:

Up to Day 42 (Phase 1 portion of study)

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: As the analysis was descriptive, no statistical analysis is provided.

End point values	Phase 1 - Cohort 1	Phase 1 - Cohort 2	Phase 1 - Cohort 3	Phase 1 - Cohort 4
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	3	3	3	10
Units: subjects	0	0	0	1

End point values	Phase 1 - Cohort 5			
Subject group type	Subject analysis set			
Number of subjects analysed	6			
Units: subjects	1			

Statistical analyses

Primary: Percentage of Subjects Achieving A Response Over the First Two Treatment Cycles in Phase 2

End point title	Percentage of Subjects Achieving A Response Over the First Two Treatment Cycles in Phase 2 ^{[3][4]}
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End point description:

Response categories 1) complete remission (CR): without circulating blasts or extramedullary disease, bone marrow (BM) with <5% blasts, and platelet (plt)/ANC recovery: $\geq 75/\geq 0.75$ [$\times 10^9/L$] 2) CR in absence of plt recovery (CRp): $\text{plt} \geq 20$ to $< 75 \times 10^9/L$ 3) partial remission (PR): no circulating blasts, appearance of normal hematopoietic progenitors, and either a BM with $\geq 5\%$ and $\leq 25\%$ blasts with recovery of plt/ANC or a BM with <5% blasts not meeting CR/CRp definition 4) Overall remission (OR): CR+CRp 5) Any response: CR+CRp+PR. All phase 2 subjects.

End point type	Primary
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End point timeframe:

Approximately 28-56 days (Phase 2 portion of study)

Notes:

[3] - 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: As the analysis was descriptive, no statistical analysis is provided.

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This outcome analysed for phase 2 treatment.

End point values	Phase 2: Clofarabine, Etoposide, Cyclophosphamide			
Subject group type	Reporting group			
Number of subjects analysed	25			
Units: percentage of total subjects				
Complete remission (CR)	28			
Complete remission/absence total platelet recovery	16			
Partial remission (PR)	12			
Overall remission (OR)	44			
Any response (CR+CRp+PR)	56			

Statistical analyses

No statistical analyses for this end point

Secondary: Summary of Subjects With Adverse Events (AEs) in Phase 1

End point title	Summary of Subjects With Adverse Events (AEs) in Phase 1
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End point description:

Number of subjects with AEs that occurred during treatment and follow-up period (45 days after last cycle). Drug-related AEs and SAEs were followed until resolved or mutually agreed by the investigator and Genzyme to discontinue reporting. AEs were classified by the investigator according to severity (graded using National Cancer Institute [NCI] Common Terminology Criteria for Adverse Events [CTCAE] version 3.0) and relationship to study drug. The severity scale is: > Grade 1=Mild, Grade 2=Moderate, Grade 3=Severe, Grade 4=Life-threatening or disabling, Grade 5=Death related to AE. All phase 1 subjects.

End point type	Secondary
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End point timeframe:

Up to 9.5 months (Phase 1 portion of study)

End point values	Phase 1 - Cohort 1	Phase 1 - Cohort 2	Phase 1 - Cohort 3	Phase 1 - Cohort 4
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	3	3	3	10
Units: subjects				
At least one AE	3	3	3	10
At least one AE related to clofarabine	3	3	3	10
At least one serious AE	3	3	3	9
At least one serious AE related to clofarabine	3	2	3	9
Discontinued study due to AE	0	0	0	0
Died	3	1	3	9
AE with the worst grade of: 1	0	0	0	0
AE with the worst grade of: 2	0	0	0	0
AE with the worst grade of: 3	2	1	1	3
AE with the worst grade of: 4	1	1	2	5
AE with the worst grade of: 5	0	1	0	2

End point values	Phase 1 - Cohort 5			
Subject group type	Subject analysis set			
Number of subjects analysed	6			
Units: subjects				
At least one AE	6			
At least one AE related to clofarabine	6			
At least one serious AE	6			
At least one serious AE related to clofarabine	5			
Discontinued study due to AE	0			
Died	5			
AE with the worst grade of: 1	0			
AE with the worst grade of: 2	0			
AE with the worst grade of: 3	3			
AE with the worst grade of: 4	2			
AE with the worst grade of: 5	1			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Achieving A Response Over the First Two Treatment Cycles in Phase 1

End point title	Percentage of Subjects Achieving A Response Over the First Two Treatment Cycles in Phase 1 ^[5]
End point description: Response categories 1) complete remission (CR): without circulating blasts or extramedullary disease, bone marrow (BM) with <5% blasts, and platelet (plt)/ANC recovery: ALL $\geq 75/ \geq 0.75$ [$\times 10^9/L$]; AML $\geq 100/ \geq 1.0$ [$\times 10^9/L$] 2) CR in absence of plt recovery (CRp): ALL plt ≥ 20 to $< 75 \times 10^9/L$; AML plt ≥ 20 to $< 100 \times 10^9/L$ 3) partial remission (PR): no circulating blasts, appearance of normal hematopoietic progenitors, and either a BM with $\geq 5\%$ and $\leq 25\%$ blasts with recovery of plt/ANC or a BM with <5% blasts not meeting CR/CRp definition 4) Overall remission (OR): CR+CRp 5) Any response: CR+CRp+PR. All phase 1 subjects.	
End point type	Secondary
End point timeframe: Approximately 2 months (Phase 1 portion of study)	

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This outcome analysed for phase 1 treatment.

End point values	Phase 1: Clofarabine, Etoposide, Cyclophosphamide			
Subject group type	Reporting group			
Number of subjects analysed	16			
Units: percentage of total subjects				
Complete remission (CR)	40			
Complete remission/absence total platelet recovery	24			
Partial remission (PR)	0			
Overall remission (OR)	64			
Any response (CR+CRp+PR)	64			

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Remission for Subjects Who Had a Response in Phase 1

End point title	Time to Remission for Subjects Who Had a Response in Phase
End point description: The weeks between start of intervention and remission as assessed by the investigator in Phase 1. Subjects who had a complete remission (CR) or complete remission with the absence of total platelet recovery (CRp) are included. Subjects in phase 1 who had an overall remission.	
End point type	Secondary
End point timeframe: up to 8 weeks (Phase 1 portion of study)	

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This outcome analysed for phase 1 treatment.

End point values	Phase 1: Clofarabine, Etoposide, Cyclophosphamide			
Subject group type	Reporting group			
Number of subjects analysed	16			
Units: weeks				
arithmetic mean (standard deviation)	4.96 (± 1.912)			

Statistical analyses

No statistical analyses for this end point

Secondary: Kaplan Meier Estimate of Duration of Remission (DOR) for Subjects Who Achieved Overall Remission (OR) in Phase 1

End point title	Kaplan Meier Estimate of Duration of Remission (DOR) for Subjects Who Achieved Overall Remission (OR) in Phase 1 ^[7]
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End point description:

Duration of response is the time from the first objective measurement of complete response (CR) or complete response with the absence of total platelet recovery (CRp) to the date of first objective documentation of disease relapse or death due to any cause, plus one day. For summary purposes, results are presented as weeks. Phase 1 subjects who achieved overall remission. Data are censored at date of last known follow-up visit.

End point type	Secondary
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End point timeframe:

Up to 2 years (Phase 1 portion of study)

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This outcome analysed for phase 1 treatment.

End point values	Phase 1: Clofarabine, Etoposide, Cyclophosphamide			
Subject group type	Reporting group			
Number of subjects analysed	16			
Units: weeks				
median (confidence interval 95%)	18.2 (12.9 to 35)			

Statistical analyses

No statistical analyses for this end point

Secondary: Kaplan Meier Estimates of Event-free Survival (EFS) for Subjects in Phase 1

End point title	Kaplan Meier Estimates of Event-free Survival (EFS) for Subjects in Phase 1 ^[8]
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End point description:

Event-free survival (EFS) is defined as the time from date of first administration of study interventions until the earliest of the following: date of death or date of first response assessment confirming relapse or date of final response assessment which fails to confirm response, plus one day. For summary purposes, results are presented as weeks. All phase 1 subjects. Data are censored at date of last known follow-up visit.

End point type	Secondary
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End point timeframe:

Up to 2 years (Phase 1 portion of study)

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: This outcome analysed for phase 1 treatment.

End point values	Phase 1: Clofarabine, Etoposide, Cyclophosphamide			
Subject group type	Reporting group			
Number of subjects analysed	25			
Units: weeks				
median (confidence interval 95%)	19.3 (12.7 to 27.1)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With 4-month Event Free Survival in Phase 1

End point title	Number of Subjects With 4-month Event Free Survival in Phase 1 ^[9]
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End point description:

Number of subjects with event-free survival at four months post first dose of therapy. A subject is considered event-free if at month 4 they have not died or had a response assessment confirming a relapse. All subjects.

End point type	Secondary
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End point timeframe:

4 months (Phase I portion of study)

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: This outcome analysed for phase 1 treatment.

End point values	Phase 1: Clofarabine, Etoposide, Cyclophosphamide			
Subject group type	Reporting group			
Number of subjects analysed	25			
Units: subjects	13			

Statistical analyses

No statistical analyses for this end point

Secondary: Kaplan Meier Estimates of Overall Survival (OS) for Subjects in Phase 1

End point title	Kaplan Meier Estimates of Overall Survival (OS) for Subjects in Phase 1 ^[10]
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End point description:

Overall survival is defined as the time from date of first administration of study interventions until date of death, plus one day. For summary purposes, results are presented as weeks. All phase 1 subjects

End point type	Secondary
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End point timeframe:

Up to 2 years (Phase 1 portion of study)

Notes:

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This outcome analysed for phase 1 treatment.

End point values	Phase 1: Clofarabine, Etoposide, Cyclophosphamide			
Subject group type	Reporting group			
Number of subjects analysed	25			
Units: weeks				
median (confidence interval 95%)	27.1 (18.3 to 42.9)			

Statistical analyses

No statistical analyses for this end point

Secondary: Summary of Subjects With Adverse Events (AEs) in Phase 2

End point title	Summary of Subjects With Adverse Events (AEs) in Phase 2 ^[11]
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End point description:

Number of subjects with AEs that occurred during treatment and follow-up period (45 days after last cycle). Drug-related AEs and SAEs were followed until resolved or mutually agreed by the investigator and Genzyme to discontinue reporting. AEs were classified by the investigator according to severity (graded using National Cancer Institute [NCI] Common Terminology Criteria for Adverse Events [CTCAE] version 3.0) and relationship to study drug. The severity scale is: > Grade 1=Mild, Grade 2=Moderate, Grade 3=Severe, Grade 4=Life-threatening or disabling, Grade 5=Death related to AE. All phase 2 subjects

End point type	Secondary
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End point timeframe:

Up to 9.5 months (Phase 2 portion of study)

Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This outcome analysed for phase 2 treatment.

End point values	Phase 2: Clofarabine, Etoposide, Cyclophosphamide			
Subject group type	Reporting group			
Number of subjects analysed	25			
Units: subjects				
At least one AE	25			
At least one AE related to clofarabine	25			
At least one serious AE	21			
At least one serious AE related to clofarabine	20			
Discontinued study due to AE	1			
Died	16			
AE with the worst grade of: 1	0			
AE with the worst grade of: 2	0			
AE with the worst grade of: 3	1			
AE with the worst grade of: 4	16			
AE with the worst grade of: 5	8			

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Remission for Subjects Who Had a Response in Phase 2

End point title	Time to Remission for Subjects Who Had a Response in Phase
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End point description:

The weeks between start of intervention and remission as assessed by the investigator in Phase 2. Subjects who had a complete remission (CR) or complete remission with the absence of total platelet recovery (CRp) are included. Subjects in phase 2 who had an overall remission.

End point type	Secondary
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End point timeframe:

up to 8 weeks (Phase 2 portion of study)

Notes:

[12] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This outcome analysed for phase 2 treatment.

End point values	Phase 2: Clofarabine, Etoposide, Cyclophosphamide			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: weeks				
arithmetic mean (standard deviation)	4.84 (± 2.092)			

Statistical analyses

No statistical analyses for this end point

Secondary: Kaplan Meier Estimate of Duration of Remission (DOR) for Subjects Who Achieved Overall Remission (OR) in Phase 2

End point title	Kaplan Meier Estimate of Duration of Remission (DOR) for Subjects Who Achieved Overall Remission (OR) in Phase 2 ^[13]
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End point description:

Duration of response is the time from the first objective measurement of complete response (CR) or complete response with the absence of total platelet recovery (CRp) to the date of first objective documentation of disease relapse or death due to any cause, plus one day. For summary purposes, results are presented as weeks. Phase 2 subjects who achieved overall remission. Data are censored at date of last known follow-up visit. 99999 represents data not estimable because values are mostly censored. Subjects with longer DORs have not relapsed, progressed, or died, therefore the upper confidence limit cannot be estimated.

End point type	Secondary
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End point timeframe:

Up to 2 years (Phase 2 portion of study)

Notes:

[13] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This outcome analysed for phase 2 treatment.

End point values	Phase 2: Clofarabine, Etoposide, Cyclophosphamide			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: weeks				
median (confidence interval 95%)	67.3 (13.4 to 99999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Kaplan Meier Estimates of Event-free Survival (EFS) for Subjects in Phase 2

End point title	Kaplan Meier Estimates of Event-free Survival (EFS) for Subjects in Phase 2 ^[14]
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End point description:

Event-free survival (EFS) is defined as the time from date of first administration of study interventions until the earliest of the following: date of death or date of first response assessment confirming relapse or date of final response assessment which fails to confirm response, plus one day. For summary purposes, results are presented as weeks. All phase 2 subjects. Data are censored at date of last known follow-up visit.

End point type	Secondary
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End point timeframe:

Up to 2 years (Phase 2 portion of study)

Notes:

[14] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This outcome analysed for phase 2 treatment.

End point values	Phase 2: Clofarabine, Etoposide, Cyclophosphamide			
Subject group type	Reporting group			
Number of subjects analysed	25			
Units: weeks				
median (confidence interval 95%)	10.7 (6.7 to 73.9)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With 4-month Event Free Survival in Phase 2

End point title	Number of Subjects With 4-month Event Free Survival in Phase 2 ^[15]
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End point description:

Number of subjects with event-free survival at four months post first dose of therapy. A subject is considered event-free if at month 4 they have not died or had a response assessment confirming a relapse. All subjects.

End point type	Secondary
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End point timeframe:

4 months (Phase 2 portion of study)

Notes:

[15] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This outcome analysed for phase 2 treatment.

End point values	Phase 2: Clofarabine, Etoposide, Cyclophosphamide			
Subject group type	Reporting group			
Number of subjects analysed	25			
Units: subjects	11			

Statistical analyses

No statistical analyses for this end point

Secondary: Kaplan Meier Estimates of Overall Survival (OS) for Subjects in Phase 2

End point title	Kaplan Meier Estimates of Overall Survival (OS) for Subjects in Phase 2 ^[16]
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End point description:

Overall survival is defined as the time from date of first administration of study interventions until date of death, plus one day. For summary purposes, results are presented as weeks. All phase 2 subjects. Data are censored at date of last known follow-up visit.

End point type	Secondary
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End point timeframe:

Up to 2 years (Phase 2 portion of study)

Notes:

[16] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This outcome analysed for phase 2 treatment.

End point values	Phase 2: Clofarabine, Etoposide, Cyclophosphamide			
Subject group type	Reporting group			
Number of subjects analysed	25			
Units: weeks				
median (confidence interval 95%)	10.7 (8.1 to 38.6)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Reported AEs are Treatment emergent adverse events and death occurred in Phase 1 from day 1 up to 9.5 months. Phase 2 also lasted up to 9.5 months and started after Phase 1.

Adverse event reporting additional description:

In the event a single subject has experienced both a serious and a non-serious form of the same adverse event term, the subject has been included in the numerator ("number of affected subjects") of adverse event tables.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	13.0
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Reporting groups

Reporting group title	Phase 1 - Cohort 1
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Reporting group description:

Subjects were treated with clofarabine 20 mg/m², etoposide 75 mg/m², and cyclophosphamide 340 mg/m².

Reporting group title	Phase 1 - Cohort 2
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Reporting group description:

Subjects were treated with clofarabine 20 mg/m², etoposide 75 mg/m², and cyclophosphamide 440 mg/m².

Reporting group title	Phase 1 - Cohort 3
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Reporting group description:

Subjects were treated with clofarabine 20 mg/m², etoposide 100 mg/m², and cyclophosphamide 440 mg/m².

Reporting group title	Phase 2: Clofarabine, Etoposide, Cyclophosphamide
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Reporting group description:

Phase 2: The recommended phase 2 doses (RP2D) were clofarabine 40 mg/m², etoposide 100 mg/m² and cyclophosphamide 440 mg/m² delivered intravenously.

Reporting group title	Phase 1 - Cohort 5
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Reporting group description:

Subjects were treated with clofarabine 40 mg/m², etoposide 100 mg/m², and cyclophosphamide 440 mg/m².

Reporting group title	Phase 1 - Total
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Reporting group description:

All subjects from Cohorts 1-5 in Phase 1

Reporting group title	Phase 1 - Cohort 4
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Reporting group description:

Subjects were treated with clofarabine 30 mg/m², etoposide 100 mg/m², and cyclophosphamide 440 mg/m².

Serious adverse events	Phase 1 - Cohort 1	Phase 1 - Cohort 2	Phase 1 - Cohort 3
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 3 (100.00%)	3 / 3 (100.00%)	3 / 3 (100.00%)
number of deaths (all causes)	3	1	3
number of deaths resulting from adverse events			

Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignant Neoplasm Progression			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Vascular disorders			
Capillary Leak Syndrome			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Hypotension			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Venooclusive Disease			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (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			
Chills			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Generalised Oedema			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (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
Mucosal Inflammation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (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 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (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 / 3 (33.33%)	0 / 3 (0.00%)	3 / 3 (100.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	4 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Drug Hypersensitivity			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (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			
Genital Rash			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (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 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoxia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (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
Pleural Effusion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Pneumothorax			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Pulmonary Haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Pulmonary Oedema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (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 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspartate Aminotransferase Increased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood Creatine Phosphokinase Increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fungal Test Positive			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (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
Lipase Increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Polyomavirus Test Positive			

subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Transfusion Reaction			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (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
Cardiac disorders			
Intracardiac Mass			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Pericardial Effusion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Ventricular Tachycardia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (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			
Cerebral Haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Convulsion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Encephalopathy			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (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

Post Herpetic Neuralgia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Bone Marrow Failure			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Disseminated Intravascular Coagulation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Febrile Neutropenia			
subjects affected / exposed	3 / 3 (100.00%)	1 / 3 (33.33%)	3 / 3 (100.00%)
occurrences causally related to treatment / all	3 / 3	2 / 2	4 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Leukocytosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Lymphopenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Neutropenia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	1 / 1	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Pancytopenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (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 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Eye disorders			
Trichiasis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal Pain			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (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
Ascites			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (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
Caecitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Enteritis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (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

Gastritis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Gingival Bleeding			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Oesophagitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Pancreatitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Rectal Fissure			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (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			
Hyperbilirubinaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (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 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (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			

Lichenoid Keratosis			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (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
Rash			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (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			
Cystitis Haemorrhagic			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematuria			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (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 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (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 Acute			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (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 Impairment			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (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			
Acinetobacter Bacteraemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (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

Alpha Haemolytic Streptococcal Infection				
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0	
Bacteraemia				
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (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	
Bacterial Sepsis				
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (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	
Bk Virus Infection				
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (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	
Bronchopulmonary Aspergillosis				
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (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	
Cellulitis				
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (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	
Central Nervous System Infection				
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (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	
Cerebral Fungal Infection				
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (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	
Clostridial Infection				

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium Difficile Colitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cystitis			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (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
Cytomegalovirus Viraemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device Related Infection			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (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
Ear Infection Fungal			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enterobacter Bacteraemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enterobacter Infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Enterococcal Bacteraemia			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Enterococcal Sepsis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Escherichia Bacteraemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Escherichia Infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes Zoster			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	4 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Human Herpesvirus 6 Infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Klebsiella Bacteraemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	3 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Klebsiella Infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Lobar Pneumonia			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Lung Infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Meningitis Bacterial			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Meningitis Streptococcal			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Otitis Media Bacterial			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (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
Pelvic Abscess			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Perirectal Abscess			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia Fungal			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Pulmonary Mycosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Sinusitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Septic Shock			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Sinusitis Fungal			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Staphylococcal Bacteraemia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Staphylococcal Infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Staphylococcal Sepsis			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (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 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Streptococcal Sepsis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper Respiratory Tract Infection			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary Tract Infection Enterococcal			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Vaginal Infection			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (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
Viraemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Wound Infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Wound Infection Staphylococcal			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Decreased Appetite			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Dehydration			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Hyperglycaemia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (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
Hypernatraemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Hyperuricaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Hypokalaemia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	2 / 2	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypophosphataemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Metabolic Acidosis			

subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tumour Lysis Syndrome			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (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	Phase 2: Clofarabine, Etoposide, Cyclophosphamide	Phase 1 - Cohort 5	Phase 1 - Total
Total subjects affected by serious adverse events			
subjects affected / exposed	21 / 25 (84.00%)	6 / 6 (100.00%)	24 / 25 (96.00%)
number of deaths (all causes)	18	6	22
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignant Neoplasm Progression			
subjects affected / exposed	0 / 25 (0.00%)	1 / 6 (16.67%)	3 / 25 (12.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 3
Vascular disorders			
Capillary Leak Syndrome			
subjects affected / exposed	4 / 25 (16.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	5 / 5	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypotension			
subjects affected / exposed	4 / 25 (16.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	3 / 4	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Venoocclusive Disease			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (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			
Chills			

subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (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
Generalised Oedema			
subjects affected / exposed	0 / 25 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
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	0 / 25 (0.00%)	0 / 6 (0.00%)	2 / 25 (8.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Multi-Organ Failure			
subjects affected / exposed	2 / 25 (8.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	3 / 25 (12.00%)	0 / 6 (0.00%)	6 / 25 (24.00%)
occurrences causally related to treatment / all	3 / 3	0 / 0	7 / 9
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Drug Hypersensitivity			
subjects affected / exposed	0 / 25 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Genital Rash			
subjects affected / exposed	0 / 25 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 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 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (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
Hypoxia			
subjects affected / exposed	1 / 25 (4.00%)	1 / 6 (16.67%)	3 / 25 (12.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural Effusion			
subjects affected / exposed	1 / 25 (4.00%)	1 / 6 (16.67%)	2 / 25 (8.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumothorax			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (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
Pulmonary Haemorrhage			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (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
Pulmonary Oedema			
subjects affected / exposed	2 / 25 (8.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Investigations			
Alanine Aminotransferase Increased			
subjects affected / exposed	2 / 25 (8.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences causally related to treatment / all	3 / 3	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspartate Aminotransferase Increased			
subjects affected / exposed	2 / 25 (8.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences causally related to treatment / all	3 / 3	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood Creatine Phosphokinase Increased			

subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fungal Test Positive			
subjects affected / exposed	0 / 25 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lipase Increased			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	2 / 25 (8.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Polyomavirus Test Positive			
subjects affected / exposed	0 / 25 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Transfusion Reaction			
subjects affected / exposed	0 / 25 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Intracardiac Mass			
subjects affected / exposed	0 / 25 (0.00%)	1 / 6 (16.67%)	1 / 25 (4.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pericardial Effusion			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ventricular Tachycardia			
subjects affected / exposed	0 / 25 (0.00%)	1 / 6 (16.67%)	1 / 25 (4.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Nervous system disorders			
Cerebral Haemorrhage			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	1 / 1	0 / 0	1 / 1
Convulsion			
subjects affected / exposed	0 / 25 (0.00%)	1 / 6 (16.67%)	2 / 25 (8.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Encephalopathy			
subjects affected / exposed	0 / 25 (0.00%)	1 / 6 (16.67%)	1 / 25 (4.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post Herpetic Neuralgia			
subjects affected / exposed	0 / 25 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 25 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bone Marrow Failure			
subjects affected / exposed	2 / 25 (8.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Disseminated Intravascular Coagulation			
subjects affected / exposed	0 / 25 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Febrile Neutropenia			
subjects affected / exposed	15 / 25 (60.00%)	3 / 6 (50.00%)	17 / 25 (68.00%)
occurrences causally related to treatment / all	15 / 17	3 / 3	25 / 25
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Leukocytosis			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (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
Lymphopenia			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (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
Neutropenia			
subjects affected / exposed	0 / 25 (0.00%)	2 / 6 (33.33%)	5 / 25 (20.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	6 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancytopenia			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (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
Thrombocytopenia			
subjects affected / exposed	0 / 25 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Eye disorders			
Trichiasis			
subjects affected / exposed	0 / 25 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal Pain			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	2 / 25 (8.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ascites			
subjects affected / exposed	0 / 25 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Caecitis			
subjects affected / exposed	3 / 25 (12.00%)	0 / 6 (0.00%)	4 / 25 (16.00%)
occurrences causally related to treatment / all	3 / 3	0 / 0	3 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	2 / 25 (8.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enteritis			
subjects affected / exposed	0 / 25 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastritis			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (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
Gingival Bleeding			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (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
Oesophagitis			
subjects affected / exposed	0 / 25 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis			
subjects affected / exposed	2 / 25 (8.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal Fissure			
subjects affected / exposed	0 / 25 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			

subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (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 disorders			
Hyperbilirubinaemia			
subjects affected / exposed	2 / 25 (8.00%)	1 / 6 (16.67%)	1 / 25 (4.00%)
occurrences causally related to treatment / all	4 / 4	2 / 2	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Venoocclusive Liver Disease			
subjects affected / exposed	3 / 25 (12.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences causally related to treatment / all	6 / 6	0 / 0	1 / 1
deaths causally related to treatment / all	2 / 2	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Lichenoid Keratosis			
subjects affected / exposed	0 / 25 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rash			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (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
Renal and urinary disorders			
Cystitis Haemorrhagic			
subjects affected / exposed	0 / 25 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematuria			
subjects affected / exposed	0 / 25 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal Failure			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (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

Renal Failure Acute			
subjects affected / exposed	3 / 25 (12.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	6 / 6	0 / 0	0 / 0
deaths causally related to treatment / all	2 / 2	0 / 0	0 / 0
Renal Impairment			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (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
Infections and infestations			
Acinetobacter Bacteraemia			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (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
Alpha Haemolytic Streptococcal Infection			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	2 / 25 (8.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bacteraemia			
subjects affected / exposed	0 / 25 (0.00%)	0 / 6 (0.00%)	2 / 25 (8.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bacterial Sepsis			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (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
Bk Virus Infection			
subjects affected / exposed	0 / 25 (0.00%)	1 / 6 (16.67%)	3 / 25 (12.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	3 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchopulmonary Aspergillosis			
subjects affected / exposed	2 / 25 (8.00%)	1 / 6 (16.67%)	1 / 25 (4.00%)
occurrences causally related to treatment / all	2 / 2	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	1 / 1	1 / 1

Cellulitis			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (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
Central Nervous System Infection			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Cerebral Fungal Infection			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (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
Clostridial Infection			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (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
Clostridium Difficile Colitis			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (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
Cystitis			
subjects affected / exposed	0 / 25 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cytomegalovirus Viraemia			
subjects affected / exposed	0 / 25 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device Related Infection			
subjects affected / exposed	2 / 25 (8.00%)	2 / 6 (33.33%)	3 / 25 (12.00%)
occurrences causally related to treatment / all	2 / 2	2 / 2	2 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear Infection Fungal			

subjects affected / exposed	0 / 25 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enterobacter Bacteraemia			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enterobacter Infection			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (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
Enterococcal Bacteraemia			
subjects affected / exposed	2 / 25 (8.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enterococcal Sepsis			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (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
Escherichia Bacteraemia			
subjects affected / exposed	2 / 25 (8.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Escherichia Infection			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (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
Herpes Zoster			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	4 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Human Herpesvirus 6 Infection			

subjects affected / exposed	0 / 25 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Klebsiella Bacteraemia			
subjects affected / exposed	0 / 25 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	3 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Klebsiella Infection			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (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
Lobar Pneumonia			
subjects affected / exposed	0 / 25 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung Infection			
subjects affected / exposed	2 / 25 (8.00%)	0 / 6 (0.00%)	2 / 25 (8.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meningitis Bacterial			
subjects affected / exposed	0 / 25 (0.00%)	1 / 6 (16.67%)	1 / 25 (4.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	1 / 1	1 / 1
Meningitis Streptococcal			
subjects affected / exposed	0 / 25 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Otitis Media Bacterial			
subjects affected / exposed	0 / 25 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pelvic Abscess			

subjects affected / exposed	0 / 25 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Perirectal Abscess			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (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
Pneumonia			
subjects affected / exposed	2 / 25 (8.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia Fungal			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (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
Pulmonary Mycosis			
subjects affected / exposed	2 / 25 (8.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	1 / 25 (4.00%)	1 / 6 (16.67%)	1 / 25 (4.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinusitis			
subjects affected / exposed	0 / 25 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic Shock			
subjects affected / exposed	4 / 25 (16.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences causally related to treatment / all	4 / 4	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Sinusitis Fungal			

subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (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
Staphylococcal Bacteraemia			
subjects affected / exposed	0 / 25 (0.00%)	0 / 6 (0.00%)	2 / 25 (8.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Staphylococcal Infection			
subjects affected / exposed	1 / 25 (4.00%)	2 / 6 (33.33%)	3 / 25 (12.00%)
occurrences causally related to treatment / all	1 / 1	3 / 3	4 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Staphylococcal Sepsis			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (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
Streptococcal Bacteraemia			
subjects affected / exposed	0 / 25 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Streptococcal Sepsis			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (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
Upper Respiratory Tract Infection			
subjects affected / exposed	0 / 25 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary Tract Infection Enterococcal			
subjects affected / exposed	1 / 25 (4.00%)	1 / 6 (16.67%)	1 / 25 (4.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vaginal Infection			

subjects affected / exposed	0 / 25 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viraemia			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (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
Wound Infection			
subjects affected / exposed	0 / 25 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound Infection Staphylococcal			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (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
Metabolism and nutrition disorders			
Decreased Appetite			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dehydration			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (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
Hyperglycaemia			
subjects affected / exposed	0 / 25 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypernatraemia			
subjects affected / exposed	0 / 25 (0.00%)	1 / 6 (16.67%)	1 / 25 (4.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperuricaemia			

subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (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
Hypokalaemia			
subjects affected / exposed	2 / 25 (8.00%)	0 / 6 (0.00%)	2 / 25 (8.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	3 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypophosphataemia			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (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
Metabolic Acidosis			
subjects affected / exposed	0 / 25 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tumour Lysis Syndrome			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (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

Serious adverse events	Phase 1 - Cohort 4		
Total subjects affected by serious adverse events			
subjects affected / exposed	9 / 10 (90.00%)		
number of deaths (all causes)	9		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignant Neoplasm Progression			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Vascular disorders			
Capillary Leak Syndrome			

subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypotension			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Venoocclusive Disease			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Chills			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Generalised Oedema			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Mucosal Inflammation			
subjects affected / exposed	2 / 10 (20.00%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Multi-Organ Failure			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pyrexia			
subjects affected / exposed	2 / 10 (20.00%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Immune system disorders			

Drug Hypersensitivity			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Genital Rash			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Acute Respiratory Distress Syndrome			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypoxia			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pleural Effusion			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumothorax			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pulmonary Haemorrhage			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pulmonary Oedema			

subjects affected / exposed	0 / 10 (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 / 10 (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 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood Creatine Phosphokinase Increased			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Fungal Test Positive			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Lipase Increased			
subjects affected / exposed	2 / 10 (20.00%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Polyomavirus Test Positive			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Transfusion Reaction			

subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Intracardiac Mass			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pericardial Effusion			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Ventricular Tachycardia			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Cerebral Haemorrhage			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	1 / 1		
Convulsion			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Encephalopathy			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Post Herpetic Neuralgia			
subjects affected / exposed	0 / 10 (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	1 / 10 (10.00%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Bone Marrow Failure				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Disseminated Intravascular Coagulation				
subjects affected / exposed	1 / 10 (10.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Febrile Neutropenia				
subjects affected / exposed	7 / 10 (70.00%)			
occurrences causally related to treatment / all	13 / 13			
deaths causally related to treatment / all	0 / 0			
Leukocytosis				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lymphopenia				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Neutropenia				
subjects affected / exposed	1 / 10 (10.00%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Pancytopenia				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Thrombocytopenia				

subjects affected / exposed	1 / 10 (10.00%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	1 / 1		
Eye disorders			
Trichiasis			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal Pain			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Ascites			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Caecitis			
subjects affected / exposed	3 / 10 (30.00%)		
occurrences causally related to treatment / all	2 / 3		
deaths causally related to treatment / all	0 / 0		
Diarrhoea			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Enteritis			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Gastritis			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gingival Bleeding			

subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Oesophagitis			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Pancreatitis			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Rectal Fissure			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vomiting			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Hyperbilirubinaemia			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Venoocclusive Liver Disease			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Lichenoid Keratosis			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Rash			

subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Cystitis Haemorrhagic			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Haematuria			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal Failure			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal Failure Acute			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal Impairment			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Acinetobacter Bacteraemia			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Alpha Haemolytic Streptococcal Infection			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

Bacteraemia				
subjects affected / exposed	2 / 10 (20.00%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Bacterial Sepsis				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bk Virus Infection				
subjects affected / exposed	1 / 10 (10.00%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Bronchopulmonary Aspergillosis				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cellulitis				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Central Nervous System Infection				
subjects affected / exposed	1 / 10 (10.00%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Cerebral Fungal Infection				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Clostridial Infection				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Clostridium Difficile Colitis				

subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cystitis				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cytomegalovirus Viraemia				
subjects affected / exposed	1 / 10 (10.00%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Device Related Infection				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ear Infection Fungal				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Enterobacter Bacteraemia				
subjects affected / exposed	1 / 10 (10.00%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Enterobacter Infection				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Enterococcal Bacteraemia				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Enterococcal Sepsis				

subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Escherichia Bacteraemia				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Escherichia Infection				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Herpes Zoster				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Human Herpesvirus 6 Infection				
subjects affected / exposed	1 / 10 (10.00%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Klebsiella Bacteraemia				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Klebsiella Infection				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lobar Pneumonia				
subjects affected / exposed	1 / 10 (10.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Lung Infection				

subjects affected / exposed	2 / 10 (20.00%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Meningitis Bacterial				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Meningitis Streptococcal				
subjects affected / exposed	1 / 10 (10.00%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Otitis Media Bacterial				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pelvic Abscess				
subjects affected / exposed	1 / 10 (10.00%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Perirectal Abscess				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia Fungal				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pulmonary Mycosis				

subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Sepsis				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Sinusitis				
subjects affected / exposed	1 / 10 (10.00%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Septic Shock				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Sinusitis Fungal				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Staphylococcal Bacteraemia				
subjects affected / exposed	1 / 10 (10.00%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Staphylococcal Infection				
subjects affected / exposed	1 / 10 (10.00%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Staphylococcal Sepsis				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Streptococcal Bacteraemia				

subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Streptococcal Sepsis			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Upper Respiratory Tract Infection			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Urinary Tract Infection Enterococcal			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vaginal Infection			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Viraemia			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Wound Infection			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Wound Infection Staphylococcal			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Decreased Appetite			

subjects affected / exposed	1 / 10 (10.00%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Dehydration				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hyperglycaemia				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypernatraemia				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hyperuricaemia				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypokalaemia				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypophosphataemia				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Metabolic Acidosis				
subjects affected / exposed	0 / 10 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Tumour Lysis Syndrome				

subjects affected / exposed	0 / 10 (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: 0 %

Non-serious adverse events	Phase 1 - Cohort 1	Phase 1 - Cohort 2	Phase 1 - Cohort 3
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 3 (100.00%)	3 / 3 (100.00%)	3 / 3 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cancer Pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Malignant Neoplasm Progression			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Penile Wart			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Flushing			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Haematoma			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypertension			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Hypotension			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	2 / 3 (66.67%)
occurrences (all)	0	0	2
General disorders and administration site conditions			
Catheter Site Erythema			

subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Application Site Rash			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Catheter Site Haematoma			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Catheter Site Pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Catheter Site Rash			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Catheter Site Related Reaction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Chills			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	2 / 3 (66.67%)
occurrences (all)	1	0	3
Chest Pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Device Occlusion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Face Oedema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Disease Progression			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	1	0	4
Feeling Abnormal			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Generalised Oedema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypothermia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Infusion Site Extravasation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Injection Site Haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Irritability			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Malaise			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Mucosal Inflammation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Non-Cardiac Chest Pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Multi-Organ Failure			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Oedema Peripheral			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pneumatosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pain			

subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Puncture Site Pain subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Pyrexia subjects affected / exposed occurrences (all)	2 / 3 (66.67%) 2	0 / 3 (0.00%) 0	1 / 3 (33.33%) 1
Immune system disorders Acute Graft Versus Host Disease subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Graft Versus Host Disease subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	1 / 3 (33.33%) 1
Drug Hypersensitivity subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Acute Graft Versus Host Disease In Intestine subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Reproductive system and breast disorders Breast Pain subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Balanitis subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	1 / 3 (33.33%) 1
Epididymal Cyst subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Metrorrhagia subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Genital Rash			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Genital Pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pelvic Haematoma			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pelvic Pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Vulvovaginal Pruritus			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pruritus Genital			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			
Alveolitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Acute Respiratory Distress Syndrome			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	2
Atelectasis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Epistaxis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	3 / 3 (100.00%)
occurrences (all)	0	0	4
Dyspnoea			
subjects affected / exposed	1 / 3 (33.33%)	2 / 3 (66.67%)	1 / 3 (33.33%)
occurrences (all)	1	2	1
Cough			

subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	1 / 3 (33.33%)
occurrences (all)	0	2	1
Haemoptysis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Hiccups			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypoxia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	3
Lung Infiltration			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nasal Congestion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal Pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Painful Respiration			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pleural Effusion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pneumothorax			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pneumonitis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Pleuritic Pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Productive Cough			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pulmonary Haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Pulmonary Oedema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Respiratory Distress			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Rhinorrhoea			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Sinus Disorder			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Sinus Congestion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Sleep Apnoea Syndrome			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Tachypnoea			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Upper Respiratory Tract Congestion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Wheezing			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 3 (33.33%)	1 / 3 (33.33%)	2 / 3 (66.67%)
occurrences (all)	1	1	6

Agitation			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	1 / 3 (33.33%)
occurrences (all)	0	1	1
Depression			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hallucination			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Insomnia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	1	0	1
Mental Status Changes			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Panic Attack			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Psychotic Disorder			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Social Avoidant Behaviour			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Investigations			
Antimicrobial Susceptibility Test Sensitive			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Antibiotic Resistant Staphylococcus Test Positive			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Alanine Aminotransferase Increased			
subjects affected / exposed	1 / 3 (33.33%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Bacterial Test Positive			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Aspergillus Test Positive			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Aspartate Aminotransferase Increased			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Blood Albumin Decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood Amylase Increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood Bicarbonate Decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood Creatinine Increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood Glucose Increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood Lactate Dehydrogenase Increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood Phosphorus Increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood Pressure Increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Candida Test Positive			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Brain Natriuretic Peptide Increased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Blood Urea Increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Cardiac Murmur			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Coagulation Test Abnormal			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Culture Stool Positive			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Cytomegalovirus Test Positive			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Enterococcus Test Positive			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	2
Fibrin D Dimer Increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Enterovirus Test Positive			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Haemoglobin Decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Fungal Test Positive			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Lipase Increased			

subjects affected / exposed	1 / 3 (33.33%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Occult Blood Positive			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	2
Protein Total Decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Polyomavirus Test Positive			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Specific Gravity Urine Abnormal			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Serum Ferritin Increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Prothrombin Time Prolonged			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Specific Gravity Urine Increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Urine Ketone Body			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Urine Output Decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Viral Test Positive			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Weight Decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural			

complications			
Allergic Transfusion Reaction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Contusion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Excoriation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Head Injury			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Incision Site Haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Joint Injury			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Joint Sprain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Post Lumbar Puncture Syndrome			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Post Procedural Haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Postoperative Wound Complication			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Procedural Pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Skin Laceration			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Subdural Haematoma			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Transfusion Reaction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Wound			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Bradycardia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Cardiac Arrest			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Cardiomyopathy			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Left Ventricular Dysfunction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Left Ventricular Hypertrophy			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Palpitations			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pericardial Effusion			
subjects affected / exposed	1 / 3 (33.33%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Tachycardia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1

Tricuspid Valve Incompetence subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Ventricular Extrasystoles subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	1 / 3 (33.33%) 1
Nervous system disorders			
Cerebral Thrombosis subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Amnesia subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Depressed Level Of Consciousness subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	1 / 3 (33.33%) 1
Dizziness subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	2 / 3 (66.67%) 2
Dysaesthesia subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Lethargy subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 3 (33.33%) 1	0 / 3 (0.00%) 0
Hydrocephalus subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Headache subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 2	0 / 3 (0.00%) 0	2 / 3 (66.67%) 3
Paraesthesia subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Syncope			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Somnolence			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Peripheral Sensory Neuropathy			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Tremor			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Bone Marrow Failure			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Anaemia			
subjects affected / exposed	1 / 3 (33.33%)	1 / 3 (33.33%)	2 / 3 (66.67%)
occurrences (all)	1	2	6
Coagulopathy			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Disseminated Intravascular Coagulation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Febrile Neutropenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Leukopenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Lymphopenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Lymphadenopathy			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Neutropenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Pancytopenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Splenomegaly			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Thrombocytopenia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	2 / 3 (66.67%)
occurrences (all)	1	0	6
Ear and labyrinth disorders			
Deafness			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Deafness Neurosensory			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Deafness Unilateral			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Ear Pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	2 / 3 (66.67%)
occurrences (all)	0	0	3
Mixed Deafness			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Eye disorders			
Conjunctival Hyperaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Diplopia			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Conjunctivitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dry Eye			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	1	0	1
Ectropion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Exophthalmos			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Eye Pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Eye Haemorrhage			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Eye Swelling			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Photophobia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Eyelid Oedema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Retinal Exudates			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Retinopathy			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Scleral Haemorrhage			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Vision Blurred			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal Distension			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Abdominal Pain			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	2	0	4
Abdominal Pain Upper			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Anal Fissure			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Ascites			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Colitis			
subjects affected / exposed	0 / 3 (0.00%)	2 / 3 (66.67%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Cheilitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Constipation			
subjects affected / exposed	2 / 3 (66.67%)	1 / 3 (33.33%)	1 / 3 (33.33%)
occurrences (all)	2	1	4
Diarrhoea			
subjects affected / exposed	2 / 3 (66.67%)	2 / 3 (66.67%)	1 / 3 (33.33%)
occurrences (all)	2	4	2
Dental Caries			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1

Dry Mouth			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dyspepsia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Faecal Incontinence			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Eructation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal Haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Gastrooesophageal Reflux Disease			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Gingival Bleeding			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	2 / 3 (66.67%)
occurrences (all)	0	0	2
Gingival Pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Haematemesis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	3
Haematochezia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Haemorrhoids			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Intestinal Dilatation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Lip Blister			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Mouth Haemorrhage			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Lip Dry			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	2 / 3 (66.67%)	2 / 3 (66.67%)	3 / 3 (100.00%)
occurrences (all)	3	2	14
Mouth Ulceration			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Oesophageal Ulcer			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Oesophagitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Oral Disorder			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Oral Pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Oral Pruritus			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Painful Defaecation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pancreatic Atrophy			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1

Pancreatitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Perianal Erythema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Proctitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Proctalgia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	2
Rectal Fissure			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Toothache			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Tongue Discolouration			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Stomatitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Vomiting			
subjects affected / exposed	2 / 3 (66.67%)	2 / 3 (66.67%)	3 / 3 (100.00%)
occurrences (all)	2	3	17
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Cholecystitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Cholestasis			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Gallbladder Disorder			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hepatic Failure			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hepatic Lesion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hepatic Steatosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Hepatomegaly			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Hepatosplenomegaly			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Hyperbilirubinaemia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	1	0	1
Jaundice			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Venoocclusive Liver Disease			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			
Acanthosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Alopecia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	2 / 3 (66.67%)
occurrences (all)	0	0	2

Blister			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Drug Eruption			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dermatitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Decubitus Ulcer			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dry Skin			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Ecchymosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	2 / 3 (66.67%)
occurrences (all)	0	0	2
Eczema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Erythema			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Palmar-Plantar Erythrodysesthesia Syndrome			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hyperhidrosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Exfoliative Rash			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Periorbital Oedema			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Petechiae			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	6
Pruritus Generalised			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	0 / 3 (0.00%)	2 / 3 (66.67%)	2 / 3 (66.67%)
occurrences (all)	0	2	6
Rash Macular			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Red Man Syndrome			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Skin Discolouration			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Rash Papular			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Skin Disorder			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Skin Exfoliation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Skin Hyperpigmentation			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Skin Lesion			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Skin Ulcer			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Renal and urinary disorders			
Cystitis Haemorrhagic			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Haemoglobinuria			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Haematuria			
subjects affected / exposed	1 / 3 (33.33%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Dysuria			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Kidney Enlargement			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Micturition Urgency			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Oliguria			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Proteinuria			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Renal Failure			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Renal Failure Acute			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Urinary Bladder Haemorrhage subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Endocrine disorders Cushingoid subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	1 / 3 (33.33%) 1
Bone Pain subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Back Pain subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Muscle Fatigue subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Flank Pain subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	1 / 3 (33.33%) 1
Muscle Twitching subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Musculoskeletal Chest Pain subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Musculoskeletal Pain subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	1 / 3 (33.33%) 1
Neck Pain subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	1 / 3 (33.33%) 2
Myalgia			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Osteopenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Pain In Extremity			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	2 / 3 (66.67%)
occurrences (all)	1	0	3
Infections and infestations			
Acinetobacter Bacteraemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Acute Sinusitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Bacteraemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Adenovirus Infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Brain Abscess			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Bk Virus Infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	2
Bronchopulmonary Aspergillosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Candiduria			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Candidiasis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Burkholderia Cepacia Complex Infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Catheter Site Cellulitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Clostridium Difficile Colitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Clostridial Infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Cellulitis			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Cytomegalovirus Chorioretinitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Conjunctivitis Infective			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Conjunctivitis Bacterial			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Cytomegalovirus Infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Cytomegalovirus Viraemia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Device Related Infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Ear Infection			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Encephalitis Cytomegalovirus			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Enterobacter Bacteraemia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Enterococcal Bacteraemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Enterococcal Infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Enterovirus Infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Enterococcal Sepsis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Escherichia Bacteraemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Escherichia Urinary Tract Infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Fungaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Herpes Zoster			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal Candidiasis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Herpes Zoster Multi-Dermatomal			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Human Herpesvirus 6 Infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Keratitis Herpetic			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Kidney Infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Lactobacillus Infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Lung Infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Mycobacterium Kansasii Infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Onychomycosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Oral Candidiasis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Otitis Media			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Otitis Media Chronic			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Pneumonia Fungal			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pneumonia Klebsiella			

subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Pseudomonal Bacteraemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pseudomonas Infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pulmonary Mycosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Respiratory Syncytial Virus Infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Respiratory Tract Infection Bacterial			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Rhinitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Sinusitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Sinusitis Fungal			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Staphylococcal Infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Staphylococcal Bacteraemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Staphylococcal Sepsis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Stenotrophomonas Infection			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Streptococcal Sepsis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Tooth Abscess			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Systemic Candida			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Upper Respiratory Tract Infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Urinary Tract Infection Bacterial			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Urinary Tract Infection Enterococcal			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Urinary Tract Infection Staphylococcal			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	2 / 3 (66.67%)
occurrences (all)	1	0	2
Viraemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Viral Upper Respiratory Tract Infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Wound Infection Staphylococcal			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			

Decreased Appetite			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	2 / 3 (66.67%)
occurrences (all)	1	0	4
Fluid Overload			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Fluid Imbalance			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Dehydration			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Fluid Retention			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypercalcaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hyperglycaemia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	1	0	1
Hyperkalaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypermagnesaemia			
subjects affected / exposed	1 / 3 (33.33%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Hypernatraemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hyperphosphataemia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	1	0	1
Hypertriglyceridaemia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0

Hypocalcaemia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Hypoalbuminaemia			
subjects affected / exposed	1 / 3 (33.33%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Hyperuricaemia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Hypokalaemia			
subjects affected / exposed	1 / 3 (33.33%)	2 / 3 (66.67%)	1 / 3 (33.33%)
occurrences (all)	1	3	5
Hypoglycaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypomagnesaemia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Metabolic Acidosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypophosphataemia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Hyponatraemia			
subjects affected / exposed	1 / 3 (33.33%)	1 / 3 (33.33%)	1 / 3 (33.33%)
occurrences (all)	1	1	1
Polydipsia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Phase 2: Clofarabine, Etoposide, Cyclophosphamide	Phase 1 - Cohort 5	Phase 1 - Total
Total subjects affected by non-serious adverse events			
subjects affected / exposed	25 / 25 (100.00%)	6 / 6 (100.00%)	25 / 25 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			

Cancer Pain			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
Malignant Neoplasm Progression			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
Penile Wart			
subjects affected / exposed	0 / 25 (0.00%)	1 / 6 (16.67%)	1 / 25 (4.00%)
occurrences (all)	0	1	1
Vascular disorders			
Flushing			
subjects affected / exposed	0 / 25 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Haematoma			
subjects affected / exposed	0 / 25 (0.00%)	1 / 6 (16.67%)	1 / 25 (4.00%)
occurrences (all)	0	1	1
Hypertension			
subjects affected / exposed	2 / 25 (8.00%)	0 / 6 (0.00%)	2 / 25 (8.00%)
occurrences (all)	2	0	2
Hypotension			
subjects affected / exposed	11 / 25 (44.00%)	2 / 6 (33.33%)	9 / 25 (36.00%)
occurrences (all)	16	2	13
General disorders and administration site conditions			
Catheter Site Erythema			
subjects affected / exposed	1 / 25 (4.00%)	1 / 6 (16.67%)	2 / 25 (8.00%)
occurrences (all)	1	2	3
Application Site Rash			
subjects affected / exposed	0 / 25 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Catheter Site Haematoma			
subjects affected / exposed	0 / 25 (0.00%)	1 / 6 (16.67%)	1 / 25 (4.00%)
occurrences (all)	0	1	1
Catheter Site Pain			
subjects affected / exposed	2 / 25 (8.00%)	1 / 6 (16.67%)	3 / 25 (12.00%)
occurrences (all)	2	1	3
Catheter Site Rash			

subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
Catheter Site Related Reaction			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
Chills			
subjects affected / exposed	4 / 25 (16.00%)	1 / 6 (16.67%)	4 / 25 (16.00%)
occurrences (all)	6	1	5
Chest Pain			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	2	0	1
Device Occlusion			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
Face Oedema			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
Disease Progression			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
Fatigue			
subjects affected / exposed	2 / 25 (8.00%)	2 / 6 (33.33%)	6 / 25 (24.00%)
occurrences (all)	2	3	10
Feeling Abnormal			
subjects affected / exposed	0 / 25 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Generalised Oedema			
subjects affected / exposed	1 / 25 (4.00%)	1 / 6 (16.67%)	1 / 25 (4.00%)
occurrences (all)	1	1	1
Hypothermia			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
Infusion Site Extravasation			
subjects affected / exposed	0 / 25 (0.00%)	1 / 6 (16.67%)	1 / 25 (4.00%)
occurrences (all)	0	1	1
Injection Site Haemorrhage			

subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
Irritability			
subjects affected / exposed	0 / 25 (0.00%)	0 / 6 (0.00%)	2 / 25 (8.00%)
occurrences (all)	0	0	2
Malaise			
subjects affected / exposed	0 / 25 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Mucosal Inflammation			
subjects affected / exposed	8 / 25 (32.00%)	3 / 6 (50.00%)	5 / 25 (20.00%)
occurrences (all)	9	3	5
Non-Cardiac Chest Pain			
subjects affected / exposed	1 / 25 (4.00%)	1 / 6 (16.67%)	1 / 25 (4.00%)
occurrences (all)	1	1	1
Multi-Organ Failure			
subjects affected / exposed	2 / 25 (8.00%)	1 / 6 (16.67%)	1 / 25 (4.00%)
occurrences (all)	2	1	1
Oedema Peripheral			
subjects affected / exposed	0 / 25 (0.00%)	1 / 6 (16.67%)	2 / 25 (8.00%)
occurrences (all)	0	1	2
Pneumatosis			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
Pain			
subjects affected / exposed	2 / 25 (8.00%)	1 / 6 (16.67%)	2 / 25 (8.00%)
occurrences (all)	2	2	3
Puncture Site Pain			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
Pyrexia			
subjects affected / exposed	13 / 25 (52.00%)	5 / 6 (83.33%)	15 / 25 (60.00%)
occurrences (all)	15	7	26
Immune system disorders			
Acute Graft Versus Host Disease			
subjects affected / exposed	1 / 25 (4.00%)	1 / 6 (16.67%)	1 / 25 (4.00%)
occurrences (all)	1	2	2

Graft Versus Host Disease subjects affected / exposed occurrences (all)	1 / 25 (4.00%) 2	0 / 6 (0.00%) 0	1 / 25 (4.00%) 1
Drug Hypersensitivity subjects affected / exposed occurrences (all)	0 / 25 (0.00%) 0	0 / 6 (0.00%) 0	2 / 25 (8.00%) 4
Acute Graft Versus Host Disease In Intestine subjects affected / exposed occurrences (all)	1 / 25 (4.00%) 1	0 / 6 (0.00%) 0	0 / 25 (0.00%) 0
Reproductive system and breast disorders			
Breast Pain subjects affected / exposed occurrences (all)	0 / 25 (0.00%) 0	1 / 6 (16.67%) 1	1 / 25 (4.00%) 1
Balanitis subjects affected / exposed occurrences (all)	0 / 25 (0.00%) 0	0 / 6 (0.00%) 0	1 / 25 (4.00%) 1
Epididymal Cyst subjects affected / exposed occurrences (all)	1 / 25 (4.00%) 1	0 / 6 (0.00%) 0	0 / 25 (0.00%) 0
Metrorrhagia subjects affected / exposed occurrences (all)	1 / 25 (4.00%) 1	0 / 6 (0.00%) 0	0 / 25 (0.00%) 0
Genital Rash subjects affected / exposed occurrences (all)	0 / 25 (0.00%) 0	0 / 6 (0.00%) 0	1 / 25 (4.00%) 3
Genital Pain subjects affected / exposed occurrences (all)	0 / 25 (0.00%) 0	0 / 6 (0.00%) 0	1 / 25 (4.00%) 3
Pelvic Haematoma subjects affected / exposed occurrences (all)	1 / 25 (4.00%) 1	0 / 6 (0.00%) 0	0 / 25 (0.00%) 0
Pelvic Pain subjects affected / exposed occurrences (all)	0 / 25 (0.00%) 0	0 / 6 (0.00%) 0	1 / 25 (4.00%) 1
Vulvovaginal Pruritus			

subjects affected / exposed	0 / 25 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Pruritus Genital			
subjects affected / exposed	0 / 25 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal disorders			
Alveolitis			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
Acute Respiratory Distress Syndrome			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	1	0	2
Atelectasis			
subjects affected / exposed	0 / 25 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Epistaxis			
subjects affected / exposed	4 / 25 (16.00%)	1 / 6 (16.67%)	7 / 25 (28.00%)
occurrences (all)	4	1	8
Dyspnoea			
subjects affected / exposed	4 / 25 (16.00%)	0 / 6 (0.00%)	4 / 25 (16.00%)
occurrences (all)	4	0	4
Cough			
subjects affected / exposed	5 / 25 (20.00%)	3 / 6 (50.00%)	7 / 25 (28.00%)
occurrences (all)	5	4	10
Haemoptysis			
subjects affected / exposed	0 / 25 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Hiccups			
subjects affected / exposed	0 / 25 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Hypoxia			
subjects affected / exposed	0 / 25 (0.00%)	1 / 6 (16.67%)	2 / 25 (8.00%)
occurrences (all)	0	1	4
Lung Infiltration			

subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
Nasal Congestion			
subjects affected / exposed	2 / 25 (8.00%)	3 / 6 (50.00%)	3 / 25 (12.00%)
occurrences (all)	2	3	3
Oropharyngeal Pain			
subjects affected / exposed	0 / 25 (0.00%)	2 / 6 (33.33%)	5 / 25 (20.00%)
occurrences (all)	0	2	5
Painful Respiration			
subjects affected / exposed	1 / 25 (4.00%)	1 / 6 (16.67%)	3 / 25 (12.00%)
occurrences (all)	1	1	3
Pleural Effusion			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	2 / 25 (8.00%)
occurrences (all)	1	0	2
Pneumothorax			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
Pneumonitis			
subjects affected / exposed	0 / 25 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Pleuritic Pain			
subjects affected / exposed	0 / 25 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Productive Cough			
subjects affected / exposed	0 / 25 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Pulmonary Haemorrhage			
subjects affected / exposed	0 / 25 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Pulmonary Oedema			
subjects affected / exposed	1 / 25 (4.00%)	1 / 6 (16.67%)	1 / 25 (4.00%)
occurrences (all)	1	1	1
Respiratory Distress			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
Rhinorrhoea			

subjects affected / exposed	4 / 25 (16.00%)	1 / 6 (16.67%)	3 / 25 (12.00%)
occurrences (all)	4	1	3
Sinus Disorder			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
Sinus Congestion			
subjects affected / exposed	0 / 25 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Sleep Apnoea Syndrome			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
Tachypnoea			
subjects affected / exposed	2 / 25 (8.00%)	0 / 6 (0.00%)	2 / 25 (8.00%)
occurrences (all)	2	0	2
Upper Respiratory Tract Congestion			
subjects affected / exposed	0 / 25 (0.00%)	1 / 6 (16.67%)	1 / 25 (4.00%)
occurrences (all)	0	1	1
Wheezing			
subjects affected / exposed	0 / 25 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Psychiatric disorders			
Anxiety			
subjects affected / exposed	3 / 25 (12.00%)	2 / 6 (33.33%)	10 / 25 (40.00%)
occurrences (all)	3	2	15
Agitation			
subjects affected / exposed	2 / 25 (8.00%)	0 / 6 (0.00%)	2 / 25 (8.00%)
occurrences (all)	2	0	2
Depression			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	1	0	1
Hallucination			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
Insomnia			
subjects affected / exposed	3 / 25 (12.00%)	1 / 6 (16.67%)	4 / 25 (16.00%)
occurrences (all)	3	1	4

Mental Status Changes subjects affected / exposed occurrences (all)	2 / 25 (8.00%) 2	0 / 6 (0.00%) 0	0 / 25 (0.00%) 0
Panic Attack subjects affected / exposed occurrences (all)	0 / 25 (0.00%) 0	1 / 6 (16.67%) 1	1 / 25 (4.00%) 1
Psychotic Disorder subjects affected / exposed occurrences (all)	0 / 25 (0.00%) 0	0 / 6 (0.00%) 0	1 / 25 (4.00%) 1
Social Avoidant Behaviour subjects affected / exposed occurrences (all)	0 / 25 (0.00%) 0	0 / 6 (0.00%) 0	1 / 25 (4.00%) 1
Investigations			
Antimicrobial Susceptibility Test Sensitive subjects affected / exposed occurrences (all)	1 / 25 (4.00%) 2	0 / 6 (0.00%) 0	0 / 25 (0.00%) 0
Antibiotic Resistant Staphylococcus Test Positive subjects affected / exposed occurrences (all)	1 / 25 (4.00%) 1	0 / 6 (0.00%) 0	0 / 25 (0.00%) 0
Alanine Aminotransferase Increased subjects affected / exposed occurrences (all)	8 / 25 (32.00%) 13	1 / 6 (16.67%) 1	3 / 25 (12.00%) 3
Bacterial Test Positive subjects affected / exposed occurrences (all)	0 / 25 (0.00%) 0	0 / 6 (0.00%) 0	1 / 25 (4.00%) 1
Aspergillus Test Positive subjects affected / exposed occurrences (all)	1 / 25 (4.00%) 1	0 / 6 (0.00%) 0	0 / 25 (0.00%) 0
Aspartate Aminotransferase Increased subjects affected / exposed occurrences (all)	11 / 25 (44.00%) 16	1 / 6 (16.67%) 2	2 / 25 (8.00%) 3
Blood Albumin Decreased subjects affected / exposed occurrences (all)	1 / 25 (4.00%) 1	0 / 6 (0.00%) 0	0 / 25 (0.00%) 0
Blood Amylase Increased			

subjects affected / exposed	2 / 25 (8.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	2	0	0
Blood Bicarbonate Decreased			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	2	0	0
Blood Creatinine Increased			
subjects affected / exposed	2 / 25 (8.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	2	0	0
Blood Glucose Increased			
subjects affected / exposed	0 / 25 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Blood Lactate Dehydrogenase Increased			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
Blood Phosphorus Increased			
subjects affected / exposed	0 / 25 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Blood Pressure Increased			
subjects affected / exposed	0 / 25 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Candida Test Positive			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	3	0	0
Brain Natriuretic Peptide Increased			
subjects affected / exposed	0 / 25 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Blood Urea Increased			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
Cardiac Murmur			
subjects affected / exposed	0 / 25 (0.00%)	1 / 6 (16.67%)	2 / 25 (8.00%)
occurrences (all)	0	1	2
Coagulation Test Abnormal			
subjects affected / exposed	0 / 25 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1

Culture Stool Positive subjects affected / exposed occurrences (all)	0 / 25 (0.00%) 0	0 / 6 (0.00%) 0	1 / 25 (4.00%) 1
Cytomegalovirus Test Positive subjects affected / exposed occurrences (all)	4 / 25 (16.00%) 4	0 / 6 (0.00%) 0	1 / 25 (4.00%) 1
Enterococcus Test Positive subjects affected / exposed occurrences (all)	0 / 25 (0.00%) 0	0 / 6 (0.00%) 0	2 / 25 (8.00%) 3
Fibrin D Dimer Increased subjects affected / exposed occurrences (all)	1 / 25 (4.00%) 1	0 / 6 (0.00%) 0	0 / 25 (0.00%) 0
Enterovirus Test Positive subjects affected / exposed occurrences (all)	0 / 25 (0.00%) 0	1 / 6 (16.67%) 1	1 / 25 (4.00%) 1
Haemoglobin Decreased subjects affected / exposed occurrences (all)	1 / 25 (4.00%) 1	1 / 6 (16.67%) 1	1 / 25 (4.00%) 1
Fungal Test Positive subjects affected / exposed occurrences (all)	0 / 25 (0.00%) 0	0 / 6 (0.00%) 0	1 / 25 (4.00%) 1
Lipase Increased subjects affected / exposed occurrences (all)	5 / 25 (20.00%) 6	0 / 6 (0.00%) 0	2 / 25 (8.00%) 2
Occult Blood Positive subjects affected / exposed occurrences (all)	1 / 25 (4.00%) 1	1 / 6 (16.67%) 1	2 / 25 (8.00%) 3
Protein Total Decreased subjects affected / exposed occurrences (all)	1 / 25 (4.00%) 1	0 / 6 (0.00%) 0	0 / 25 (0.00%) 0
Polyomavirus Test Positive subjects affected / exposed occurrences (all)	0 / 25 (0.00%) 0	0 / 6 (0.00%) 0	1 / 25 (4.00%) 1
Specific Gravity Urine Abnormal subjects affected / exposed occurrences (all)	1 / 25 (4.00%) 1	0 / 6 (0.00%) 0	0 / 25 (0.00%) 0

Serum Ferritin Increased subjects affected / exposed occurrences (all)	1 / 25 (4.00%) 1	0 / 6 (0.00%) 0	0 / 25 (0.00%) 0
Prothrombin Time Prolonged subjects affected / exposed occurrences (all)	2 / 25 (8.00%) 2	0 / 6 (0.00%) 0	1 / 25 (4.00%) 1
Specific Gravity Urine Increased subjects affected / exposed occurrences (all)	0 / 25 (0.00%) 0	1 / 6 (16.67%) 2	2 / 25 (8.00%) 3
Urine Ketone Body subjects affected / exposed occurrences (all)	1 / 25 (4.00%) 1	0 / 6 (0.00%) 0	0 / 25 (0.00%) 0
Urine Output Decreased subjects affected / exposed occurrences (all)	0 / 25 (0.00%) 0	1 / 6 (16.67%) 1	2 / 25 (8.00%) 2
Viral Test Positive subjects affected / exposed occurrences (all)	1 / 25 (4.00%) 1	0 / 6 (0.00%) 0	0 / 25 (0.00%) 0
Weight Decreased subjects affected / exposed occurrences (all)	1 / 25 (4.00%) 1	0 / 6 (0.00%) 0	0 / 25 (0.00%) 0
Injury, poisoning and procedural complications			
Allergic Transfusion Reaction subjects affected / exposed occurrences (all)	0 / 25 (0.00%) 0	1 / 6 (16.67%) 1	1 / 25 (4.00%) 1
Contusion subjects affected / exposed occurrences (all)	2 / 25 (8.00%) 2	0 / 6 (0.00%) 0	1 / 25 (4.00%) 1
Excoriation subjects affected / exposed occurrences (all)	2 / 25 (8.00%) 2	0 / 6 (0.00%) 0	0 / 25 (0.00%) 0
Head Injury subjects affected / exposed occurrences (all)	1 / 25 (4.00%) 1	0 / 6 (0.00%) 0	0 / 25 (0.00%) 0
Incision Site Haemorrhage			

subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
Joint Injury			
subjects affected / exposed	0 / 25 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Joint Sprain			
subjects affected / exposed	0 / 25 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Post Lumbar Puncture Syndrome			
subjects affected / exposed	0 / 25 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Post Procedural Haemorrhage			
subjects affected / exposed	2 / 25 (8.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	2	0	0
Postoperative Wound Complication			
subjects affected / exposed	0 / 25 (0.00%)	1 / 6 (16.67%)	1 / 25 (4.00%)
occurrences (all)	0	1	1
Procedural Pain			
subjects affected / exposed	3 / 25 (12.00%)	2 / 6 (33.33%)	4 / 25 (16.00%)
occurrences (all)	3	2	4
Skin Laceration			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
Subdural Haematoma			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
Transfusion Reaction			
subjects affected / exposed	2 / 25 (8.00%)	0 / 6 (0.00%)	2 / 25 (8.00%)
occurrences (all)	2	0	3
Wound			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
Cardiac disorders			
Bradycardia			
subjects affected / exposed	0 / 25 (0.00%)	1 / 6 (16.67%)	1 / 25 (4.00%)
occurrences (all)	0	1	1

Cardiac Arrest			
subjects affected / exposed	0 / 25 (0.00%)	1 / 6 (16.67%)	1 / 25 (4.00%)
occurrences (all)	0	2	2
Cardiomyopathy			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
Left Ventricular Dysfunction			
subjects affected / exposed	0 / 25 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Left Ventricular Hypertrophy			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
Palpitations			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
Pericardial Effusion			
subjects affected / exposed	4 / 25 (16.00%)	0 / 6 (0.00%)	3 / 25 (12.00%)
occurrences (all)	4	0	3
Tachycardia			
subjects affected / exposed	7 / 25 (28.00%)	2 / 6 (33.33%)	6 / 25 (24.00%)
occurrences (all)	9	2	7
Tricuspid Valve Incompetence			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
Ventricular Extrasystoles			
subjects affected / exposed	0 / 25 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Nervous system disorders			
Cerebral Thrombosis			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
Amnesia			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
Depressed Level Of Consciousness			

subjects affected / exposed	0 / 25 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Dizziness			
subjects affected / exposed	2 / 25 (8.00%)	1 / 6 (16.67%)	7 / 25 (28.00%)
occurrences (all)	3	1	7
Dysaesthesia			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
Lethargy			
subjects affected / exposed	0 / 25 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Hydrocephalus			
subjects affected / exposed	0 / 25 (0.00%)	1 / 6 (16.67%)	1 / 25 (4.00%)
occurrences (all)	0	1	1
Headache			
subjects affected / exposed	9 / 25 (36.00%)	4 / 6 (66.67%)	14 / 25 (56.00%)
occurrences (all)	13	5	20
Paraesthesia			
subjects affected / exposed	0 / 25 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Syncope			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
Somnolence			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
Peripheral Sensory Neuropathy			
subjects affected / exposed	0 / 25 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Tremor			
subjects affected / exposed	2 / 25 (8.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	2	0	0
Blood and lymphatic system disorders			
Bone Marrow Failure			
subjects affected / exposed	0 / 25 (0.00%)	1 / 6 (16.67%)	1 / 25 (4.00%)
occurrences (all)	0	1	1

Anaemia			
subjects affected / exposed	16 / 25 (64.00%)	2 / 6 (33.33%)	7 / 25 (28.00%)
occurrences (all)	27	4	18
Coagulopathy			
subjects affected / exposed	3 / 25 (12.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	3	0	0
Disseminated Intravascular Coagulation			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
Febrile Neutropenia			
subjects affected / exposed	5 / 25 (20.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	6	0	1
Leukopenia			
subjects affected / exposed	4 / 25 (16.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	9	0	1
Lymphopenia			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	1	0	1
Lymphadenopathy			
subjects affected / exposed	0 / 25 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Neutropenia			
subjects affected / exposed	13 / 25 (52.00%)	0 / 6 (0.00%)	3 / 25 (12.00%)
occurrences (all)	19	0	3
Pancytopenia			
subjects affected / exposed	3 / 25 (12.00%)	1 / 6 (16.67%)	2 / 25 (8.00%)
occurrences (all)	3	1	3
Splenomegaly			
subjects affected / exposed	2 / 25 (8.00%)	0 / 6 (0.00%)	3 / 25 (12.00%)
occurrences (all)	2	0	3
Thrombocytopenia			
subjects affected / exposed	16 / 25 (64.00%)	3 / 6 (50.00%)	11 / 25 (44.00%)
occurrences (all)	27	4	21
Ear and labyrinth disorders			

Deafness			
subjects affected / exposed	0 / 25 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Deafness Neurosensory			
subjects affected / exposed	0 / 25 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Deafness Unilateral			
subjects affected / exposed	0 / 25 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Ear Pain			
subjects affected / exposed	0 / 25 (0.00%)	1 / 6 (16.67%)	4 / 25 (16.00%)
occurrences (all)	0	1	5
Mixed Deafness			
subjects affected / exposed	0 / 25 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Eye disorders			
Conjunctival Hyperaemia			
subjects affected / exposed	0 / 25 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Diplopia			
subjects affected / exposed	0 / 25 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Conjunctivitis			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
Dry Eye			
subjects affected / exposed	0 / 25 (0.00%)	0 / 6 (0.00%)	2 / 25 (8.00%)
occurrences (all)	0	0	2
Ectropion			
subjects affected / exposed	0 / 25 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Exophthalmos			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
Eye Pain			

subjects affected / exposed	0 / 25 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Eye Haemorrhage			
subjects affected / exposed	0 / 25 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Eye Swelling			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
Photophobia			
subjects affected / exposed	0 / 25 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Eyelid Oedema			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
Retinal Exudates			
subjects affected / exposed	0 / 25 (0.00%)	1 / 6 (16.67%)	1 / 25 (4.00%)
occurrences (all)	0	1	1
Retinopathy			
subjects affected / exposed	0 / 25 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Scleral Haemorrhage			
subjects affected / exposed	1 / 25 (4.00%)	1 / 6 (16.67%)	1 / 25 (4.00%)
occurrences (all)	1	1	1
Vision Blurred			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			
Abdominal Distension			
subjects affected / exposed	1 / 25 (4.00%)	1 / 6 (16.67%)	2 / 25 (8.00%)
occurrences (all)	1	3	4
Abdominal Pain			
subjects affected / exposed	7 / 25 (28.00%)	2 / 6 (33.33%)	13 / 25 (52.00%)
occurrences (all)	12	2	22
Abdominal Pain Upper			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	3 / 25 (12.00%)
occurrences (all)	1	0	4

Anal Fissure			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	1	0	1
Ascites			
subjects affected / exposed	4 / 25 (16.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	4	0	1
Colitis			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	2 / 25 (8.00%)
occurrences (all)	1	0	2
Cheilitis			
subjects affected / exposed	0 / 25 (0.00%)	1 / 6 (16.67%)	1 / 25 (4.00%)
occurrences (all)	0	1	1
Constipation			
subjects affected / exposed	5 / 25 (20.00%)	1 / 6 (16.67%)	9 / 25 (36.00%)
occurrences (all)	6	1	13
Diarrhoea			
subjects affected / exposed	7 / 25 (28.00%)	5 / 6 (83.33%)	17 / 25 (68.00%)
occurrences (all)	10	8	26
Dental Caries			
subjects affected / exposed	1 / 25 (4.00%)	2 / 6 (33.33%)	5 / 25 (20.00%)
occurrences (all)	1	2	5
Dry Mouth			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
Dyspepsia			
subjects affected / exposed	0 / 25 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Faecal Incontinence			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
Eructation			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal Haemorrhage			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	1	0	1

Gastroesophageal Reflux Disease subjects affected / exposed occurrences (all)	1 / 25 (4.00%) 1	1 / 6 (16.67%) 1	2 / 25 (8.00%) 2
Gingival Bleeding subjects affected / exposed occurrences (all)	3 / 25 (12.00%) 3	0 / 6 (0.00%) 0	3 / 25 (12.00%) 3
Gingival Pain subjects affected / exposed occurrences (all)	0 / 25 (0.00%) 0	0 / 6 (0.00%) 0	1 / 25 (4.00%) 1
Haematemesis subjects affected / exposed occurrences (all)	3 / 25 (12.00%) 3	0 / 6 (0.00%) 0	2 / 25 (8.00%) 4
Haematochezia subjects affected / exposed occurrences (all)	1 / 25 (4.00%) 1	0 / 6 (0.00%) 0	0 / 25 (0.00%) 0
Haemorrhoids subjects affected / exposed occurrences (all)	1 / 25 (4.00%) 1	0 / 6 (0.00%) 0	1 / 25 (4.00%) 1
Intestinal Dilatation subjects affected / exposed occurrences (all)	1 / 25 (4.00%) 1	0 / 6 (0.00%) 0	0 / 25 (0.00%) 0
Lip Blister subjects affected / exposed occurrences (all)	0 / 25 (0.00%) 0	0 / 6 (0.00%) 0	1 / 25 (4.00%) 1
Mouth Haemorrhage subjects affected / exposed occurrences (all)	1 / 25 (4.00%) 1	1 / 6 (16.67%) 1	2 / 25 (8.00%) 2
Lip Dry subjects affected / exposed occurrences (all)	0 / 25 (0.00%) 0	1 / 6 (16.67%) 1	1 / 25 (4.00%) 1
Nausea subjects affected / exposed occurrences (all)	20 / 25 (80.00%) 35	5 / 6 (83.33%) 7	21 / 25 (84.00%) 52
Mouth Ulceration subjects affected / exposed occurrences (all)	0 / 25 (0.00%) 0	0 / 6 (0.00%) 0	2 / 25 (8.00%) 3

Oesophageal Ulcer			
subjects affected / exposed	0 / 25 (0.00%)	1 / 6 (16.67%)	1 / 25 (4.00%)
occurrences (all)	0	1	1
Oesophagitis			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
Oral Disorder			
subjects affected / exposed	2 / 25 (8.00%)	1 / 6 (16.67%)	1 / 25 (4.00%)
occurrences (all)	2	1	1
Oral Pain			
subjects affected / exposed	3 / 25 (12.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	3	0	0
Oral Pruritus			
subjects affected / exposed	0 / 25 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Painful Defaecation			
subjects affected / exposed	0 / 25 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Pancreatic Atrophy			
subjects affected / exposed	0 / 25 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Pancreatitis			
subjects affected / exposed	3 / 25 (12.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	3	0	0
Perianal Erythema			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
Proctitis			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
Proctalgia			
subjects affected / exposed	3 / 25 (12.00%)	1 / 6 (16.67%)	3 / 25 (12.00%)
occurrences (all)	3	1	4
Rectal Fissure			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	1	0	1

Toothache			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
Tongue Discolouration			
subjects affected / exposed	0 / 25 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Stomatitis			
subjects affected / exposed	3 / 25 (12.00%)	0 / 6 (0.00%)	3 / 25 (12.00%)
occurrences (all)	3	0	3
Vomiting			
subjects affected / exposed	22 / 25 (88.00%)	6 / 6 (100.00%)	22 / 25 (88.00%)
occurrences (all)	37	6	56
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
Cholecystitis			
subjects affected / exposed	2 / 25 (8.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	2	0	0
Cholestasis			
subjects affected / exposed	2 / 25 (8.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	2	0	0
Gallbladder Disorder			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
Hepatic Failure			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
Hepatic Lesion			
subjects affected / exposed	0 / 25 (0.00%)	1 / 6 (16.67%)	1 / 25 (4.00%)
occurrences (all)	0	1	1
Hepatic Steatosis			
subjects affected / exposed	0 / 25 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Hepatomegaly			

subjects affected / exposed	5 / 25 (20.00%)	0 / 6 (0.00%)	4 / 25 (16.00%)
occurrences (all)	6	0	4
Hepatosplenomegaly			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	1	0	1
Hyperbilirubinaemia			
subjects affected / exposed	6 / 25 (24.00%)	0 / 6 (0.00%)	3 / 25 (12.00%)
occurrences (all)	7	0	3
Jaundice			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
Venoocclusive Liver Disease			
subjects affected / exposed	2 / 25 (8.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	2	0	1
Skin and subcutaneous tissue disorders			
Acanthosis			
subjects affected / exposed	0 / 25 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Alopecia			
subjects affected / exposed	4 / 25 (16.00%)	1 / 6 (16.67%)	6 / 25 (24.00%)
occurrences (all)	4	1	7
Blister			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
Drug Eruption			
subjects affected / exposed	0 / 25 (0.00%)	1 / 6 (16.67%)	1 / 25 (4.00%)
occurrences (all)	0	1	1
Dermatitis			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
Decubitus Ulcer			
subjects affected / exposed	2 / 25 (8.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	2	0	0
Dry Skin			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	1	0	1

Ecchymosis			
subjects affected / exposed	2 / 25 (8.00%)	1 / 6 (16.67%)	4 / 25 (16.00%)
occurrences (all)	2	1	4
Eczema			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
Erythema			
subjects affected / exposed	6 / 25 (24.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	6	0	1
Palmar-Plantar Erythrodysaesthesia Syndrome			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
Hyperhidrosis			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	2	0	0
Exfoliative Rash			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	2	0	0
Periorbital Oedema			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
Petechiae			
subjects affected / exposed	3 / 25 (12.00%)	0 / 6 (0.00%)	3 / 25 (12.00%)
occurrences (all)	3	0	3
Pruritus			
subjects affected / exposed	6 / 25 (24.00%)	2 / 6 (33.33%)	8 / 25 (32.00%)
occurrences (all)	6	2	13
Pruritus Generalised			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
Rash			
subjects affected / exposed	4 / 25 (16.00%)	4 / 6 (66.67%)	14 / 25 (56.00%)
occurrences (all)	6	5	26
Rash Macular			

subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
Red Man Syndrome			
subjects affected / exposed	0 / 25 (0.00%)	1 / 6 (16.67%)	1 / 25 (4.00%)
occurrences (all)	0	1	1
Skin Discolouration			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
Rash Papular			
subjects affected / exposed	0 / 25 (0.00%)	1 / 6 (16.67%)	2 / 25 (8.00%)
occurrences (all)	0	1	2
Skin Disorder			
subjects affected / exposed	0 / 25 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	2
Skin Exfoliation			
subjects affected / exposed	0 / 25 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	2
Skin Hyperpigmentation			
subjects affected / exposed	1 / 25 (4.00%)	1 / 6 (16.67%)	2 / 25 (8.00%)
occurrences (all)	1	1	2
Skin Lesion			
subjects affected / exposed	0 / 25 (0.00%)	1 / 6 (16.67%)	1 / 25 (4.00%)
occurrences (all)	0	2	2
Skin Ulcer			
subjects affected / exposed	0 / 25 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Renal and urinary disorders			
Cystitis Haemorrhagic			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
Haemoglobinuria			
subjects affected / exposed	0 / 25 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Haematuria			
subjects affected / exposed	6 / 25 (24.00%)	2 / 6 (33.33%)	4 / 25 (16.00%)
occurrences (all)	7	4	6

Dysuria			
subjects affected / exposed	0 / 25 (0.00%)	0 / 6 (0.00%)	2 / 25 (8.00%)
occurrences (all)	0	0	2
Kidney Enlargement			
subjects affected / exposed	2 / 25 (8.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	2	0	0
Micturition Urgency			
subjects affected / exposed	0 / 25 (0.00%)	1 / 6 (16.67%)	1 / 25 (4.00%)
occurrences (all)	0	1	1
Oliguria			
subjects affected / exposed	2 / 25 (8.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	2	0	0
Proteinuria			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	1	0	1
Renal Failure			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
Renal Failure Acute			
subjects affected / exposed	2 / 25 (8.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	2	0	0
Urinary Bladder Haemorrhage			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
Endocrine disorders			
Cushingoid			
subjects affected / exposed	0 / 25 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	5 / 25 (20.00%)	0 / 6 (0.00%)	2 / 25 (8.00%)
occurrences (all)	5	0	2
Bone Pain			
subjects affected / exposed	1 / 25 (4.00%)	1 / 6 (16.67%)	1 / 25 (4.00%)
occurrences (all)	1	1	1
Back Pain			

subjects affected / exposed	1 / 25 (4.00%)	1 / 6 (16.67%)	3 / 25 (12.00%)
occurrences (all)	1	1	3
Muscle Fatigue			
subjects affected / exposed	0 / 25 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Flank Pain			
subjects affected / exposed	0 / 25 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Muscle Twitching			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal Chest Pain			
subjects affected / exposed	0 / 25 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Musculoskeletal Pain			
subjects affected / exposed	4 / 25 (16.00%)	0 / 6 (0.00%)	2 / 25 (8.00%)
occurrences (all)	4	0	3
Neck Pain			
subjects affected / exposed	0 / 25 (0.00%)	1 / 6 (16.67%)	4 / 25 (16.00%)
occurrences (all)	0	1	5
Myalgia			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
Osteopenia			
subjects affected / exposed	3 / 25 (12.00%)	0 / 6 (0.00%)	2 / 25 (8.00%)
occurrences (all)	3	0	2
Pain In Extremity			
subjects affected / exposed	6 / 25 (24.00%)	3 / 6 (50.00%)	11 / 25 (44.00%)
occurrences (all)	9	3	15
Infections and infestations			
Acinetobacter Bacteraemia			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
Acute Sinusitis			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0

Bacteraemia			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
Adenovirus Infection			
subjects affected / exposed	0 / 25 (0.00%)	0 / 6 (0.00%)	2 / 25 (8.00%)
occurrences (all)	0	0	2
Brain Abscess			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
Bk Virus Infection			
subjects affected / exposed	3 / 25 (12.00%)	2 / 6 (33.33%)	4 / 25 (16.00%)
occurrences (all)	4	2	5
Bronchopulmonary Aspergillosis			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
Candiduria			
subjects affected / exposed	0 / 25 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Candidiasis			
subjects affected / exposed	0 / 25 (0.00%)	0 / 6 (0.00%)	3 / 25 (12.00%)
occurrences (all)	0	0	3
Burkholderia Cepacia Complex Infection			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
Catheter Site Cellulitis			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
Clostridium Difficile Colitis			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	3	0	0
Clostridial Infection			
subjects affected / exposed	2 / 25 (8.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	2	0	0
Cellulitis			

subjects affected / exposed	3 / 25 (12.00%)	1 / 6 (16.67%)	2 / 25 (8.00%)
occurrences (all)	3	1	2
Cytomegalovirus Chorioretinitis			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
Conjunctivitis Infective			
subjects affected / exposed	0 / 25 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Conjunctivitis Bacterial			
subjects affected / exposed	0 / 25 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Cytomegalovirus Infection			
subjects affected / exposed	2 / 25 (8.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	2	0	0
Cytomegalovirus Viraemia			
subjects affected / exposed	3 / 25 (12.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	4	0	1
Device Related Infection			
subjects affected / exposed	0 / 25 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Ear Infection			
subjects affected / exposed	0 / 25 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Encephalitis Cytomegalovirus			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
Enterobacter Bacteraemia			
subjects affected / exposed	2 / 25 (8.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	2	0	1
Enterococcal Bacteraemia			
subjects affected / exposed	2 / 25 (8.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	3	0	0
Enterococcal Infection			
subjects affected / exposed	2 / 25 (8.00%)	0 / 6 (0.00%)	2 / 25 (8.00%)
occurrences (all)	2	0	3
Enterovirus Infection			

subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	2	0	0
Enterococcal Sepsis			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
Escherichia Bacteraemia			
subjects affected / exposed	2 / 25 (8.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	2	0	0
Escherichia Urinary Tract Infection			
subjects affected / exposed	0 / 25 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	2
Fungaemia			
subjects affected / exposed	0 / 25 (0.00%)	1 / 6 (16.67%)	1 / 25 (4.00%)
occurrences (all)	0	1	1
Herpes Zoster			
subjects affected / exposed	1 / 25 (4.00%)	1 / 6 (16.67%)	1 / 25 (4.00%)
occurrences (all)	1	1	1
Gastrointestinal Candidiasis			
subjects affected / exposed	0 / 25 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Herpes Zoster Multi-Dermatomal			
subjects affected / exposed	0 / 25 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Human Herpesvirus 6 Infection			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	1	0	1
Keratitis Herpetic			
subjects affected / exposed	0 / 25 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Kidney Infection			
subjects affected / exposed	0 / 25 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Lactobacillus Infection			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
Lung Infection			

subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
Mycobacterium Kansasii Infection			
subjects affected / exposed	0 / 25 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Onychomycosis			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
Oral Candidiasis			
subjects affected / exposed	3 / 25 (12.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	3	0	0
Otitis Media			
subjects affected / exposed	0 / 25 (0.00%)	0 / 6 (0.00%)	2 / 25 (8.00%)
occurrences (all)	0	0	2
Otitis Media Chronic			
subjects affected / exposed	0 / 25 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Pneumonia Fungal			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
Pneumonia Klebsiella			
subjects affected / exposed	0 / 25 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Pseudomonal Bacteraemia			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	2	0	0
Pseudomonas Infection			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
Pulmonary Mycosis			
subjects affected / exposed	1 / 25 (4.00%)	1 / 6 (16.67%)	2 / 25 (8.00%)
occurrences (all)	1	1	2
Respiratory Syncytial Virus Infection			
subjects affected / exposed	0 / 25 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Respiratory Tract Infection Bacterial			

subjects affected / exposed	1 / 25 (4.00%)	1 / 6 (16.67%)	1 / 25 (4.00%)
occurrences (all)	2	1	1
Rhinitis			
subjects affected / exposed	0 / 25 (0.00%)	1 / 6 (16.67%)	2 / 25 (8.00%)
occurrences (all)	0	1	3
Sinusitis			
subjects affected / exposed	4 / 25 (16.00%)	0 / 6 (0.00%)	2 / 25 (8.00%)
occurrences (all)	4	0	2
Sinusitis Fungal			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
Staphylococcal Infection			
subjects affected / exposed	1 / 25 (4.00%)	1 / 6 (16.67%)	2 / 25 (8.00%)
occurrences (all)	1	1	2
Staphylococcal Bacteraemia			
subjects affected / exposed	3 / 25 (12.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	6	0	1
Staphylococcal Sepsis			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
Stenotrophomonas Infection			
subjects affected / exposed	0 / 25 (0.00%)	1 / 6 (16.67%)	1 / 25 (4.00%)
occurrences (all)	0	1	1
Streptococcal Sepsis			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
Tooth Abscess			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
Systemic Candida			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
Upper Respiratory Tract Infection			
subjects affected / exposed	0 / 25 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Urinary Tract Infection Bacterial			

subjects affected / exposed	0 / 25 (0.00%)	1 / 6 (16.67%)	1 / 25 (4.00%)
occurrences (all)	0	1	1
Urinary Tract Infection Enterococcal			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
Urinary Tract Infection Staphylococcal			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	4 / 25 (16.00%)
occurrences (all)	1	0	4
Viraemia			
subjects affected / exposed	4 / 25 (16.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	6	0	0
Viral Upper Respiratory Tract Infection			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
Wound Infection Staphylococcal			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
Metabolism and nutrition disorders			
Decreased Appetite			
subjects affected / exposed	15 / 25 (60.00%)	4 / 6 (66.67%)	12 / 25 (48.00%)
occurrences (all)	16	6	18
Fluid Overload			
subjects affected / exposed	0 / 25 (0.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	0	0	1
Fluid Imbalance			
subjects affected / exposed	1 / 25 (4.00%)	1 / 6 (16.67%)	3 / 25 (12.00%)
occurrences (all)	1	1	3
Dehydration			
subjects affected / exposed	2 / 25 (8.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	2	0	0
Fluid Retention			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
Hypercalcaemia			

subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
Hyperglycaemia			
subjects affected / exposed	4 / 25 (16.00%)	0 / 6 (0.00%)	3 / 25 (12.00%)
occurrences (all)	5	0	3
Hyperkalaemia			
subjects affected / exposed	2 / 25 (8.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	3	0	0
Hypermagnesaemia			
subjects affected / exposed	0 / 25 (0.00%)	0 / 6 (0.00%)	2 / 25 (8.00%)
occurrences (all)	0	0	2
Hypernatraemia			
subjects affected / exposed	2 / 25 (8.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	2	0	0
Hyperphosphataemia			
subjects affected / exposed	4 / 25 (16.00%)	0 / 6 (0.00%)	2 / 25 (8.00%)
occurrences (all)	4	0	2
Hypertriglyceridaemia			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	2 / 25 (8.00%)
occurrences (all)	1	0	2
Hypocalcaemia			
subjects affected / exposed	6 / 25 (24.00%)	1 / 6 (16.67%)	3 / 25 (12.00%)
occurrences (all)	6	1	4
Hypoalbuminaemia			
subjects affected / exposed	3 / 25 (12.00%)	0 / 6 (0.00%)	2 / 25 (8.00%)
occurrences (all)	3	0	2
Hyperuricaemia			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	1 / 25 (4.00%)
occurrences (all)	1	0	1
Hypokalaemia			
subjects affected / exposed	15 / 25 (60.00%)	1 / 6 (16.67%)	11 / 25 (44.00%)
occurrences (all)	21	2	20
Hypoglycaemia			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0
Hypomagnesaemia			

subjects affected / exposed	5 / 25 (20.00%)	1 / 6 (16.67%)	5 / 25 (20.00%)
occurrences (all)	6	1	5
Metabolic Acidosis			
subjects affected / exposed	2 / 25 (8.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	2	0	0
Hypophosphataemia			
subjects affected / exposed	8 / 25 (32.00%)	1 / 6 (16.67%)	3 / 25 (12.00%)
occurrences (all)	10	1	3
Hyponatraemia			
subjects affected / exposed	7 / 25 (28.00%)	2 / 6 (33.33%)	6 / 25 (24.00%)
occurrences (all)	8	2	6
Polydipsia			
subjects affected / exposed	1 / 25 (4.00%)	0 / 6 (0.00%)	0 / 25 (0.00%)
occurrences (all)	1	0	0

Non-serious adverse events	Phase 1 - Cohort 4		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	10 / 10 (100.00%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cancer Pain			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Malignant Neoplasm Progression			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Penile Wart			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Vascular disorders			
Flushing			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Haematoma			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Hypertension			

subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Hypotension			
subjects affected / exposed	5 / 10 (50.00%)		
occurrences (all)	9		
General disorders and administration site conditions			
Catheter Site Erythema			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Application Site Rash			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Catheter Site Haematoma			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Catheter Site Pain			
subjects affected / exposed	2 / 10 (20.00%)		
occurrences (all)	2		
Catheter Site Rash			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Catheter Site Related Reaction			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Chills			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Chest Pain			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Device Occlusion			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Face Oedema			

subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Disease Progression			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Fatigue			
subjects affected / exposed	2 / 10 (20.00%)		
occurrences (all)	2		
Feeling Abnormal			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Generalised Oedema			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Hypothermia			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Infusion Site Extravasation			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Injection Site Haemorrhage			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Irritability			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Malaise			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Mucosal Inflammation			
subjects affected / exposed	2 / 10 (20.00%)		
occurrences (all)	2		
Non-Cardiac Chest Pain			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Multi-Organ Failure			

subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Oedema Peripheral			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Pneumatosis			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Pain			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Puncture Site Pain			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Pyrexia			
subjects affected / exposed	7 / 10 (70.00%)		
occurrences (all)	16		
Immune system disorders			
Acute Graft Versus Host Disease			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Graft Versus Host Disease			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Drug Hypersensitivity			
subjects affected / exposed	2 / 10 (20.00%)		
occurrences (all)	4		
Acute Graft Versus Host Disease In Intestine			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Reproductive system and breast disorders			
Breast Pain			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Balanitis			

subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Epididymal Cyst			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Metrorrhagia			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Genital Rash			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	3		
Genital Pain			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	3		
Pelvic Haematoma			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Pelvic Pain			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Vulvovaginal Pruritus			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Pruritus Genital			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal disorders			
Alveolitis			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Acute Respiratory Distress Syndrome			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Atelectasis			

subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Epistaxis			
subjects affected / exposed	3 / 10 (30.00%)		
occurrences (all)	3		
Dyspnoea			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Cough			
subjects affected / exposed	2 / 10 (20.00%)		
occurrences (all)	3		
Haemoptysis			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Hiccups			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Hypoxia			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Lung Infiltration			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Nasal Congestion			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Oropharyngeal Pain			
subjects affected / exposed	3 / 10 (30.00%)		
occurrences (all)	3		
Painful Respiration			
subjects affected / exposed	2 / 10 (20.00%)		
occurrences (all)	2		
Pleural Effusion			
subjects affected / exposed	2 / 10 (20.00%)		
occurrences (all)	2		
Pneumothorax			

subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Pneumonitis			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Pleuritic Pain			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Productive Cough			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Pulmonary Haemorrhage			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Pulmonary Oedema			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Respiratory Distress			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Rhinorrhoea			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Sinus Disorder			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Sinus Congestion			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Sleep Apnoea Syndrome			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Tachypnoea			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Upper Respiratory Tract Congestion			

subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Wheezing			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Psychiatric disorders			
Anxiety			
subjects affected / exposed	4 / 10 (40.00%)		
occurrences (all)	5		
Agitation			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Depression			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Hallucination			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Insomnia			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Mental Status Changes			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Panic Attack			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Psychotic Disorder			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Social Avoidant Behaviour			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Investigations			
Antimicrobial Susceptibility Test Sensitive			

subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Antibiotic Resistant Staphylococcus Test Positive			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Alanine Aminotransferase Increased			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Bacterial Test Positive			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Aspergillus Test Positive			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Aspartate Aminotransferase Increased			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Blood Albumin Decreased			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Blood Amylase Increased			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Blood Bicarbonate Decreased			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Blood Creatinine Increased			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Blood Glucose Increased			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Blood Lactate Dehydrogenase Increased			

subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Blood Phosphorus Increased			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Blood Pressure Increased			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Candida Test Positive			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Brain Natriuretic Peptide Increased			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Blood Urea Increased			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Cardiac Murmur			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Coagulation Test Abnormal			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Culture Stool Positive			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Cytomegalovirus Test Positive			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Enterococcus Test Positive			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Fibrin D Dimer Increased			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Enterovirus Test Positive			

subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Haemoglobin Decreased			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Fungal Test Positive			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Lipase Increased			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Occult Blood Positive			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Protein Total Decreased			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Polyomavirus Test Positive			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Specific Gravity Urine Abnormal			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Serum Ferritin Increased			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Prothrombin Time Prolonged			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Specific Gravity Urine Increased			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Urine Ketone Body			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Urine Output Decreased			

subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Viral Test Positive			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Weight Decreased			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Injury, poisoning and procedural complications			
Allergic Transfusion Reaction			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Contusion			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Excoriation			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Head Injury			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Incision Site Haemorrhage			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Joint Injury			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Joint Sprain			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Post Lumbar Puncture Syndrome			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Post Procedural Haemorrhage			

subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Postoperative Wound Complication			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Procedural Pain			
subjects affected / exposed	2 / 10 (20.00%)		
occurrences (all)	2		
Skin Laceration			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Subdural Haematoma			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Transfusion Reaction			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	2		
Wound			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Cardiac disorders			
Bradycardia			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Cardiac Arrest			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Cardiomyopathy			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Left Ventricular Dysfunction			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Left Ventricular Hypertrophy			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		

Palpitations			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Pericardial Effusion			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Tachycardia			
subjects affected / exposed	3 / 10 (30.00%)		
occurrences (all)	4		
Tricuspid Valve Incompetence			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Ventricular Extrasystoles			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Cerebral Thrombosis			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Amnesia			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Depressed Level Of Consciousness			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Dizziness			
subjects affected / exposed	4 / 10 (40.00%)		
occurrences (all)	4		
Dysaesthesia			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Lethargy			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Hydrocephalus			

subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Headache			
subjects affected / exposed	7 / 10 (70.00%)		
occurrences (all)	10		
Paraesthesia			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Syncope			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Somnolence			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Peripheral Sensory Neuropathy			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Tremor			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Blood and lymphatic system disorders			
Bone Marrow Failure			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Anaemia			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	5		
Coagulopathy			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Disseminated Intravascular Coagulation			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Febrile Neutropenia			

subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Leukopenia			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Lymphopenia			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Lymphadenopathy			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Neutropenia			
subjects affected / exposed	2 / 10 (20.00%)		
occurrences (all)	2		
Pancytopenia			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	2		
Splenomegaly			
subjects affected / exposed	3 / 10 (30.00%)		
occurrences (all)	3		
Thrombocytopenia			
subjects affected / exposed	5 / 10 (50.00%)		
occurrences (all)	10		
Ear and labyrinth disorders			
Deafness			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Deafness Neurosensory			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Deafness Unilateral			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Ear Pain			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		

Mixed Deafness subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0		
Eye disorders			
Conjunctival Hyperaemia subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0		
Diplopia subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0		
Conjunctivitis subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0		
Dry Eye subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0		
Ectropion subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0		
Exophthalmos subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0		
Eye Pain subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0		
Eye Haemorrhage subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0		
Eye Swelling subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0		
Photophobia subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0		
Eyelid Oedema			

subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Retinal Exudates			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Retinopathy			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Scleral Haemorrhage			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Vision Blurred			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Abdominal Distension			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Abdominal Pain			
subjects affected / exposed	9 / 10 (90.00%)		
occurrences (all)	14		
Abdominal Pain Upper			
subjects affected / exposed	2 / 10 (20.00%)		
occurrences (all)	3		
Anal Fissure			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Ascites			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Colitis			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Cheilitis			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		

Constipation			
subjects affected / exposed	4 / 10 (40.00%)		
occurrences (all)	5		
Diarrhoea			
subjects affected / exposed	7 / 10 (70.00%)		
occurrences (all)	10		
Dental Caries			
subjects affected / exposed	2 / 10 (20.00%)		
occurrences (all)	2		
Dry Mouth			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Dyspepsia			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Faecal Incontinence			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Eructation			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Gastrointestinal Haemorrhage			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Gastrooesophageal Reflux Disease			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Gingival Bleeding			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Gingival Pain			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Haematemesis			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		

Haematochezia			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Haemorrhoids			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Intestinal Dilatation			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Lip Blister			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Mouth Haemorrhage			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Lip Dry			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Nausea			
subjects affected / exposed	9 / 10 (90.00%)		
occurrences (all)	26		
Mouth Ulceration			
subjects affected / exposed	2 / 10 (20.00%)		
occurrences (all)	3		
Oesophageal Ulcer			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Oesophagitis			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Oral Disorder			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Oral Pain			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		

Oral Pruritus			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Painful Defaecation			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Pancreatic Atrophy			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Pancreatitis			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Perianal Erythema			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Proctitis			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Proctalgia			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Rectal Fissure			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Toothache			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Tongue Discolouration			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Stomatitis			
subjects affected / exposed	2 / 10 (20.00%)		
occurrences (all)	2		
Vomiting			
subjects affected / exposed	9 / 10 (90.00%)		
occurrences (all)	28		

Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Cholecystitis			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Cholestasis			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Gallbladder Disorder			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Hepatic Failure			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Hepatic Lesion			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Hepatic Steatosis			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Hepatomegaly			
subjects affected / exposed	3 / 10 (30.00%)		
occurrences (all)	3		
Hepatosplenomegaly			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Hyperbilirubinaemia			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Jaundice			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Venoocclusive Liver Disease			

subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Skin and subcutaneous tissue disorders			
Acanthosis			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Alopecia			
subjects affected / exposed	3 / 10 (30.00%)		
occurrences (all)	4		
Blister			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Drug Eruption			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Dermatitis			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Decubitus Ulcer			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Dry Skin			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Ecchymosis			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Eczema			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Erythema			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Palmar-Plantar Erythrodysesthesia Syndrome			

subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Hyperhidrosis			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Exfoliative Rash			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Periorbital Oedema			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Petechiae			
subjects affected / exposed	3 / 10 (30.00%)		
occurrences (all)	3		
Pruritus			
subjects affected / exposed	5 / 10 (50.00%)		
occurrences (all)	5		
Pruritus Generalised			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Rash			
subjects affected / exposed	6 / 10 (60.00%)		
occurrences (all)	13		
Rash Macular			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Red Man Syndrome			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Skin Discolouration			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Rash Papular			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Skin Disorder			

subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	2		
Skin Exfoliation			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	2		
Skin Hyperpigmentation			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Skin Lesion			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Skin Ulcer			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Renal and urinary disorders			
Cystitis Haemorrhagic			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Haemoglobinuria			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Haematuria			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Dysuria			
subjects affected / exposed	2 / 10 (20.00%)		
occurrences (all)	2		
Kidney Enlargement			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Micturition Urgency			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Oliguria			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		

Proteinuria			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Renal Failure			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Renal Failure Acute			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Urinary Bladder Haemorrhage			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Endocrine disorders			
Cushingoid			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Bone Pain			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Back Pain			
subjects affected / exposed	2 / 10 (20.00%)		
occurrences (all)	2		
Muscle Fatigue			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Flank Pain			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Muscle Twitching			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Musculoskeletal Chest Pain			

subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Musculoskeletal Pain			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	2		
Neck Pain			
subjects affected / exposed	2 / 10 (20.00%)		
occurrences (all)	2		
Myalgia			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Osteopenia			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Pain In Extremity			
subjects affected / exposed	5 / 10 (50.00%)		
occurrences (all)	8		
Infections and infestations			
Acinetobacter Bacteraemia			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Acute Sinusitis			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Bacteraemia			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Adenovirus Infection			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Brain Abscess			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Bk Virus Infection			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		

Bronchopulmonary Aspergillosis			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Candiduria			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Candidiasis			
subjects affected / exposed	3 / 10 (30.00%)		
occurrences (all)	3		
Burkholderia Cepacia Complex Infection			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Catheter Site Cellulitis			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Clostridium Difficile Colitis			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Clostridial Infection			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Cellulitis			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Cytomegalovirus Chorioretinitis			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Conjunctivitis Infective			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Conjunctivitis Bacterial			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Cytomegalovirus Infection			

subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Cytomegalovirus Viraemia			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Device Related Infection			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Ear Infection			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Encephalitis Cytomegalovirus			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Enterobacter Bacteraemia			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Enterococcal Bacteraemia			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Enterococcal Infection			
subjects affected / exposed	2 / 10 (20.00%)		
occurrences (all)	3		
Enterovirus Infection			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Enterococcal Sepsis			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Escherichia Bacteraemia			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Escherichia Urinary Tract Infection			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	2		
Fungaemia			

subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Herpes Zoster			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Gastrointestinal Candidiasis			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Herpes Zoster Multi-Dermatomal			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Human Herpesvirus 6 Infection			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Keratitis Herpetic			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Kidney Infection			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Lactobacillus Infection			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Lung Infection			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Mycobacterium Kansasii Infection			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Onychomycosis			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Oral Candidiasis			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Otitis Media			

subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Otitis Media Chronic			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Pneumonia Fungal			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Pneumonia Klebsiella			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Pseudomonal Bacteraemia			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Pseudomonas Infection			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Pulmonary Mycosis			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Respiratory Syncytial Virus Infection			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Respiratory Tract Infection Bacterial			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Rhinitis			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	2		
Sinusitis			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Sinusitis Fungal			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Staphylococcal Infection			

subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Staphylococcal Bacteraemia			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Staphylococcal Sepsis			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Stenotrophomonas Infection			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Streptococcal Sepsis			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Tooth Abscess			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Systemic Candida			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Upper Respiratory Tract Infection			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Urinary Tract Infection Bacterial			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Urinary Tract Infection Enterococcal			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Urinary Tract Infection Staphylococcal			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Viraemia			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		

Viral Upper Respiratory Tract Infection			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Wound Infection Staphylococcal			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Metabolism and nutrition disorders			
Decreased Appetite			
subjects affected / exposed	5 / 10 (50.00%)		
occurrences (all)	7		
Fluid Overload			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Fluid Imbalance			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Dehydration			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Fluid Retention			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Hypercalcaemia			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Hyperglycaemia			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Hyperkalaemia			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Hypermagnesaemia			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Hypernatraemia			

subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Hyperphosphataemia			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Hypertriglyceridaemia			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Hypocalcaemia			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	2		
Hypoalbuminaemia			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Hyperuricaemia			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Hypokalaemia			
subjects affected / exposed	6 / 10 (60.00%)		
occurrences (all)	9		
Hypoglycaemia			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Hypomagnesaemia			
subjects affected / exposed	3 / 10 (30.00%)		
occurrences (all)	3		
Metabolic Acidosis			
subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		
Hypophosphataemia			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Hyponatraemia			
subjects affected / exposed	1 / 10 (10.00%)		
occurrences (all)	1		
Polydipsia			

subjects affected / exposed	0 / 10 (0.00%)		
occurrences (all)	0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
27 January 2006	- Rationale for the increased monitoring of serum amylase and lipase was added. - An expanded rationale for performing the proposed combination study was provided. - Phase 2 Primary Objective was changed as: To estimate the response rate (CR + CRp) at the RP2D in this study population. - Following Phase 2 secondary endpoint was added: The rate of any response (CR + CRp + PR) in the study population. - More detail has been added to specify when a subject might have a second induction cycle. A statement was added to suggest repeating a bone marrow aspirate/biopsy if it was performed following recent granulocyte colony stimulating factor (G-CSF) use. - Dose Modifications were done during the Treatment Period (Intracycle Dose Modifications) and for Subsequent Cycles of Study Treatment (Intercycle Dose Modifications) - A bone marrow aspirate was to be assessed for gene expression profiles, minimal residual disease and nucleoside transporter assay. The window for performing the first bone marrow biopsy/aspirate following induction was increased by one week to allow more time for blood count recovery. - Table for Response Rate Confidence Intervals was added. - Intention-To-Treat (ITT) population and Expanded ITT (E-ITT) population were defined. - The definition of Event-Free Survival, Relapse, Partial Response and Any Response were clarified.
09 November 2006	- The rationale for selection of the target doses for etoposide and cyclophosphamide was added. - The timing for administration of prophylactic IT MTX was clarified. - A dose range for G-CSF was added. - The period for assessing bone marrow following induction cycle 1 was clarified, i.e., between days 14 to day 21. - Due to the complexity of determining dose-limiting toxicities in this three-drug combination study a process elaborating the determination of DLTs was added. - The timing of baseline evaluations was clarified by the addition of "prior" to Day 1. - The timing for collection of peripheral blood smears and for assessment of the best response were clarified. - The number of subjects was increased from 39 to 40 as an additional subject was added to the Phase 2 part of the study. - The definition of intent-to-treat (ITT) population was revised. Initially, a subject was required to receive one dose of each of the three study drugs to be included in the ITT population. That requirement was revised to one dose of clofarabine only.

25 January 2008	- Extended the study period to approximately 30 months to allow for the pause in enrollment and the extra time needed to enroll a higher number of subjects in this amendment. - Removed the Phase 1 and 2 secondary objectives and related endpoints to characterize the pharmacodynamics of intracellular clofarabine triphosphate. - Changed the number of subjects to approximately 58 total subjects, 25 subjects in Phase 1, and 33 subjects in Phase 2. - The subject populations for efficacy analyses were decreased to 2 based on the revised study design. - Information about measuring the pharmacokinetics of clofarabine triphosphate was changed. - Infection prophylaxis was revised to provide more comprehensive treatment guidelines. - Methods and schedule for optional pharmacokinetic testing was added to provide a more complete picture of the hepatotoxicity seen in Phase 2. - Uric acid was added to the serum chemistries panel during Days 2 through 5 of each cycle for clarification. - The definition of relapsed AML was changed to $\geq 5\%$ leukemic blasts for consistency. - The reporting of all AEs and SAEs was changed to 45 days after discontinuing study drug (rather than study treatment), for clarification.
21 July 2009	- The number of subjects needed for enrollment in the Phase 2 portion of the study was decreased from 33 to 25. - Reinduction cycle was added to the timepoint for minimal residual disease (MRD) assessment. MRD samples were to be collected at study entry, Day 28 bone marrow assessment at the end of induction cycle one, at the Day 28 bone marrow assessment at the end of reinduction, and the first bone marrow aspiration performed after consolidation timepoints. - A third population (secondary efficacy analysis subjects) was added for efficacy analysis in order to capture and analyze data for Phase 2 subjects with no prior history of hematopoietic stem cell transplant (HSCT). - The follow-up period for subjects was changed from 2 years to a minimum of 4 months and maximum of 2 years after final study visit. - Evaluation of HSV antibody serology at baseline was clarified to state that it should only be conducted if the test at original diagnosis was negative or if there was no documentation that a HSV antibody serology test had been performed. - Hepatitis B/C screening evaluation was further clarified as hepatitis B surface antigen/hepatitis C antibody. - Assessment of gene profiling at time of relapse was added to the final study visit and follow-up assessment.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported