Clinical trial results:
A Phase 1 Dose Escalation, Open-Label Study of Venetoclax in Combination with Navitoclax and Chemotherapy in Subjects with Relapsed/Refractory Acute Lymphoblastic Leukemia or Relapsed/Refractory Lymphoblastic Lymphoma

Summary

EudraCT number	2017-001541-26
Trial protocol	Outside EU/EEA
Global end of trial date	14 November 2020

Results information

Result version number	v1 (current)
This version publication date	20 June 2021
First version publication date	20 June 2021

Trial information

Trial identification

Sponsor protocol code	M16-106

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03181126
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	AbbVie
Sponsor organisation address	1 North Waukegan Road, North Chicago, IL, United States, 60064
Public contact	Global Medical Services, AbbVie, 001 800-633-9110, abbvieclinicaltrials@abbvie.com
Scientific contact	Global Medical Services, AbbVie, 001 800-633-9110, abbvieclinicaltrials@abbvie.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	14 November 2020
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	14 November 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objectives of the study were:
- Evaluate the safety of venetoclax in combination with navitoclax;
- Evaluate the safety of venetoclax in combination with navitoclax and chemotherapy;
- Determine dose-limiting toxicities (DLTs) of venetoclax, navitoclax, and chemotherapy;
- Assess the pharmacokinetics (PK) of venetoclax in combination with navitoclax.

Protection of trial subjects:

Subject and/or legal guardian read and understood the information provided about the study and gave written permission.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	27 November 2017
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	Australia: 11
Country: Number of subjects enrolled	United States: 58
Worldwide total number of subjects	69
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)	0
Children (2-11 years)	12
Adolescents (12-17 years)	6
Adults (18-64 years)	45
From 65 to 84 years	6

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This was an open-label, Phase 1 dose escalation study in pediatric and adult patients with relapsed/refractory (R/R) acute lymphoblastic leukemia (ALL) or R/R lymphoblastic lymphoma (LL). The study was conducted at 14 sites in the United States and Australia.

Pre-assignment

Screening details:

Dose escalation decisions were guided by Bayesian optimal interval design, which utilized a decision rule within each weight group (< 45 kg and ≥ 45 kg) based on cumulative numbers of patients who experienced a dose-limiting toxicity (DLT).

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	Venetoclax + Navitoclax 25 mg

Arm description:

Participants ≥ 45 kg received oral venetoclax daily, adjusted by weight, to match the exposure of the adult equivalent target doses of 200 mg on Day 1 and 400 mg on Day 2 and onwards for up to 37 weeks. From Day 3 participants also received oral navitoclax 25 mg administered daily. Participants may have received chemotherapy from Day 1 for up to 2 cycles at the discretion of the Investigator.

Arm type	Experimental
Investigational medicinal product name	Venetoclax
Investigational medicinal product code	ABT-199 (GDC-0199)
Other name	VENCLEXTA®
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Administered orally once a day at a dose adjusted by weight to match the exposure of the adult equivalent target doses of 200 mg on Day 1 and 400 mg on Day 2 onwards.

Investigational medicinal product name	Navitoclax
Investigational medicinal product code	ABT-263
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Navitoclax was administered orally once a day based on patient weight; dose level 1 was 25 mg for patients ≥ 45 kg only.

Investigational medicinal product name	Chemotherapy
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion, Tablet
Routes of administration	Intravenous use, Oral use

Dosage and administration details:

The recommended chemotherapy schedule consisted of:
- PEG-asparaginase 1250 IU/m^2 intravenous (IV) or intramuscular equivalent on days 1 and 15;
- vincristine 1.5 mg/m^2 (maximum 2 mg) IV weekly on days 1, 8, 15, and 22;
- dexamethasone 20 mg/m^2/day orally divided twice daily on days 1–5 and 15–19.

Arm title	Venetoclax + Navitoclax 50 mg

Arm description:

Participants received oral venetoclax daily, adjusted by weight, to match the exposure of the adult equivalent target doses of 200 mg on Day 1 and 400 mg on Day 2 onwards for up to 37 weeks. From Day 3 participants also received oral navitoclax 50 mg (or 25 mg for subjects weighing < 45 kg) administered daily. Participants may have received chemotherapy from Day 1 for up to 2 cycles at the discretion of the Investigator.

Arm type	Experimental
Investigational medicinal product name	Venetoclax
Investigational medicinal product code	ABT-199 (GDC-0199)
Other name	VENCLEXTA®
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Administered orally once a day at a dose adjusted by weight to match the exposure of the adult equivalent target doses of 200 mg on Day 1 and 400 mg from Day 2 and thereafter.

Investigational medicinal product name	Navitoclax
Investigational medicinal product code	ABT-263
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Navitoclax was administered orally once a day based on patient weight; dose level 2 was 50 mg for ≥45 kg and 25 mg for 20 kg to <45 kg.

Investigational medicinal product name	Chemotherapy
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion, Tablet
Routes of administration	Intravenous use, Oral use

Dosage and administration details:

The recommended chemotherapy schedule consisted of:
- PEG-asparaginase 1250 IU/m^2 intravenous (IV) or intramuscular equivalent on days 1 and 15;
- vincristine 1.5 mg/m^2 (maximum 2 mg) IV weekly on days 1, 8, 15, and 22;
- dexamethasone 20 mg/m^2/day orally divided twice daily on days 1–5 and 15–19.

Arm title	Venetoclax + Navitoclax 100 mg

Arm description:

Participants received oral venetoclax daily, adjusted by weight, to match the exposure of the adult equivalent target doses of 200 mg on Day 1 and 400 mg on Day 2 onwards for up to 37 weeks. From Day 3 participants also received oral navitoclax 100 mg (50 mg for subjects weighing < 45 kg) administered daily. Participants may have received chemotherapy from Day 1 for up to 2 cycles at the discretion of the Investigator.

Arm type	Experimental
Investigational medicinal product name	Venetoclax
Investigational medicinal product code	ABT-199 (GDC-0199)
Other name	VENCLEXTA®
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Administered orally once a day at a dose adjusted by weight to match the exposure of the adult equivalent target doses of 200 mg on Day 1 and 400 mg from Day 2 and thereafter.

Investigational medicinal product name	Navitoclax
Investigational medicinal product code	ABT-263
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Navitoclax was administered orally once a day based on patient weight; dose level 3 was 100 mg for ≥ 45 kg and 50 mg for 20 kg to < 45 kg.

Investigational medicinal product name	Chemotherapy
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion, Tablet
Routes of administration	Intravenous use, Oral use

Dosage and administration details:

The recommended chemotherapy schedule consisted of:
- PEG-asparaginase 1250 IU/m^2 intravenous (IV) or intramuscular equivalent on days 1 and 15;
- vincristine 1.5 mg/m^2 (maximum 2 mg) IV weekly on days 1, 8, 15, and 22;
- dexamethasone 20 mg/m^2/day orally divided twice daily on days 1–5 and 15–19.

Arm title	Safety Expansion

Arm description:

Participants received oral venetoclax, adjusted by weight to match the exposure of the adult equivalent target dose of 400 mg daily and oral navitoclax 50 mg (25 mg for subjects weighing < 45 kg) administered daily for 21 days of every 28 days. Participants may have received chemotherapy from Day 1 for up to 2 cycles at the discretion of the Investigator.

Arm type	Experimental
Investigational medicinal product name	Venetoclax
Investigational medicinal product code	ABT-199 (GDC-0199)
Other name	VENCLEXTA®
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Administered orally once a day at a dose adjusted by weight to match the exposure of the adult equivalent target dose of 400 mg.

Investigational medicinal product name	Navitoclax
Investigational medicinal product code	ABT-263
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Navitoclax was administered orally at 50 mg daily for subjects weighing ≥ 45 kg or 25 mg daily for subjects weighing < 45 kg.

Investigational medicinal product name	Chemotherapy
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion, Tablet
Routes of administration	Intravenous use, Oral use

Dosage and administration details:

The recommended chemotherapy schedule consisted of:
- PEG-asparaginase 1250 IU/m^2 IV or intramuscular equivalent on days 1 and 15;
- vincristine 1.5 mg/m^2 (maximum 2 mg) IV weekly on days 1, 8, 15, and 22;
- dexamethasone 20 mg/m^2/day orally divided twice daily on days 1–5 and 15–19.

Number of subjects in period 1	Venetoclax + Navitoclax 25 mg	Venetoclax + Navitoclax 50 mg	Venetoclax + Navitoclax 100 mg
Started	16	11	20
Received venetoclax	16	11	20
Received navitoclax	16	11	19
Completed	0	0	0
Not completed	16	11	20
Consent withdrawn by subject	-	-	-
Death	13	7	14
Study terminated by sponsor	3	4	5
Non-compliance	-	-	1

Number of subjects in period 1	Safety Expansion
Started	22
Received venetoclax	22
Received navitoclax	22
Completed	0
Not completed	22
Consent withdrawn by subject	1
Death	15
Study terminated by sponsor	6
Non-compliance	-

Baseline characteristics

Reporting groups	
Reporting group title	Venetoclax + Navitoclax 25 mg
Reporting group description:	
Participants ≥ 45 kg received oral venetoclax daily, adjusted by weight, to match the exposure of the adult equivalent target doses of 200 mg on Day 1 and 400 mg on Day 2 and onwards for up to 37 weeks. From Day 3 participants also received oral navitoclax 25 mg administered daily. Participants may have received chemotherapy from Day 1 for up to 2 cycles at the discretion of the Investigator.	
Reporting group title	Venetoclax + Navitoclax 50 mg
Reporting group description:	
Participants received oral venetoclax daily, adjusted by weight, to match the exposure of the adult equivalent target doses of 200 mg on Day 1 and 400 mg on Day 2 onwards for up to 37 weeks. From Day 3 participants also received oral navitoclax 50 mg (or 25 mg for subjects weighing < 45 kg) administered daily. Participants may have received chemotherapy from Day 1 for up to 2 cycles at the discretion of the Investigator.	
Reporting group title	Venetoclax + Navitoclax 100 mg
Reporting group description:	
Participants received oral venetoclax daily, adjusted by weight, to match the exposure of the adult equivalent target doses of 200 mg on Day 1 and 400 mg on Day 2 onwards for up to 37 weeks. From Day 3 participants also received oral navitoclax 100 mg (50 mg for subjects weighing < 45 kg) administered daily. Participants may have received chemotherapy from Day 1 for up to 2 cycles at the discretion of the Investigator.	
Reporting group title	Safety Expansion
Reporting group description:	
Participants received oral venetoclax, adjusted by weight to match the exposure of the adult equivalent target dose of 400 mg daily and oral navitoclax 50 mg (25 mg for subjects weighing < 45 kg) administered daily for 21 days of every 28 days. Participants may have received chemotherapy from Day 1 for up to 2 cycles at the discretion of the Investigator.	

Reporting group values	Venetoclax + Navitoclax 25 mg	Venetoclax + Navitoclax 50 mg	Venetoclax + Navitoclax 100 mg
Number of subjects	16	11	20
Age categorical			
Units: Subjects			
Age continuous			
Units: years			
median	30	20	28
full range (min-max)	14 to 45	6 to 72	6 to 72
Gender categorical			
Units: Subjects			
Female	4	4	10
Male	12	7	10
Race			
Units: Subjects			
White	11	9	16
Black or African American	2	1	0
Asian	1	0	2
American Indian or Alaska Native	0	0	0
Native Hawaiian or Other Pacific Islander	0	1	0
Missing	2	0	2
Type of Primary Cancer			

Units: Subjects			
Acute lymphoblastic leukemia	16	9	19
Lymphoblastic lymphoma	0	2	1

Reporting group values	Safety Expansion	Total	
Number of subjects	22	69	
Age categorical Units: Subjects			
Age continuous Units: years			
median	28		
full range (min-max)	6 to 72	-	
Gender categorical Units: Subjects			
Female	7	25	
Male	15	44	
Race Units: Subjects			
White	17	53	
Black or African American	1	4	
Asian	3	6	
American Indian or Alaska Native	0	0	
Native Hawaiian or Other Pacific Islander	0	1	
Missing	1	5	
Type of Primary Cancer Units: Subjects			
Acute lymphoblastic leukemia	19	63	
Lymphoblastic lymphoma	3	6	

End points

End points reporting groups

Reporting group title	Venetoclax + Navitoclax 25 mg
Reporting group description:	
Participants ≥ 45 kg received oral venetoclax daily, adjusted by weight, to match the exposure of the adult equivalent target doses of 200 mg on Day 1 and 400 mg on Day 2 and onwards for up to 37 weeks. From Day 3 participants also received oral navitoclax 25 mg administered daily. Participants may have received chemotherapy from Day 1 for up to 2 cycles at the discretion of the Investigator.	
Reporting group title	Venetoclax + Navitoclax 50 mg
Reporting group description:	
Participants received oral venetoclax daily, adjusted by weight, to match the exposure of the adult equivalent target doses of 200 mg on Day 1 and 400 mg on Day 2 onwards for up to 37 weeks. From Day 3 participants also received oral navitoclax 50 mg (or 25 mg for subjects weighing < 45 kg) administered daily. Participants may have received chemotherapy from Day 1 for up to 2 cycles at the discretion of the Investigator.	
Reporting group title	Venetoclax + Navitoclax 100 mg
Reporting group description:	
Participants received oral venetoclax daily, adjusted by weight, to match the exposure of the adult equivalent target doses of 200 mg on Day 1 and 400 mg on Day 2 onwards for up to 37 weeks. From Day 3 participants also received oral navitoclax 100 mg (50 mg for subjects weighing < 45 kg) administered daily. Participants may have received chemotherapy from Day 1 for up to 2 cycles at the discretion of the Investigator.	
Reporting group title	Safety Expansion
Reporting group description:	
Participants received oral venetoclax, adjusted by weight to match the exposure of the adult equivalent target dose of 400 mg daily and oral navitoclax 50 mg (25 mg for subjects weighing < 45 kg) administered daily for 21 days of every 28 days. Participants may have received chemotherapy from Day 1 for up to 2 cycles at the discretion of the Investigator.	
Subject analysis set title	Total
Subject analysis set type	Safety analysis
Subject analysis set description:	
All enrolled participants who received venetoclax and navitoclax.	
Subject analysis set title	Pediatric
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Subjects aged < 18 years.	
Subject analysis set title	Adult
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Subjects aged ≥ 18 years	
Subject analysis set title	B-ALL
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Subjects with B-cell acute lymphoblastic leukemia.	
Subject analysis set title	T-ALL
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Subjects with T-cell acute lymphoblastic leukemia.	
Subject analysis set title	LL
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Subjects with lymphoblastic lymphoma.	

Primary: Number of Participants with Dose-limiting Toxicities (DLTs)

End point title	Number of Participants with Dose-limiting Toxicities (DLTs)[1][2]

End point description:

Subjects must have received at least 75% of venetoclax and navitoclax doses during the first 28 days or have experienced a DLT to be deemed evaluable for DLTs.
Any Grade 3 or higher non-hematologic adverse event (AE) that concurs with the administration of venetoclax, navitoclax, or chemotherapy was considered a dose limiting toxicity except:
- AEs that the Investigator determined are clearly due to an identifiable cause such as disease progression, underlying illness, and concurrent illness;
- AEs related to a chemotherapy agent only (no causality to venetoclax or navitoclax) which are common and expected as determined by the Investigator and are managed
- Grade 3 nausea, vomiting or diarrhea that is adequately managed with supportive care;
- Infection;
- Fever;
-Electrolyte or laboratory abnormalities that resolve to Grade ≤ 2 within 7 days, without evidence of end organ damage, including those related to tumor lysis syndrome (TLS);
- Clinical tumor lysis syndrome

End point type	Primary

End point timeframe:

First 28 days of treatment

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Statistical analyses were not conducted.

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Subjects in the safety expansion cohort were not evaluated for DLTs.

End point values	Venetoclax + Navitoclax 25 mg	Venetoclax + Navitoclax 50 mg	Venetoclax + Navitoclax 100 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	15[3]	10[4]	13[5]	
Units: participants	1	2	5	

Notes:

[3] - DLT evaluable

[4] - DLT evaluable

[5] - DLT evaluable

Statistical analyses

No statistical analyses for this end point

Primary: Maximum Observed Plasma Concentration (Cmax) of Venetoclax

End point title	Maximum Observed Plasma Concentration (Cmax) of Venetoclax[6]

End point description:

Plasma concentrations of venetoclax were determined using a validated liquid/liquid extraction followed by high performance liquid chromatography with tandem mass spectrometric detection. The lower limit of quantitation (LLOQ) and upper limit of quantitation (ULOQ) were established at 2.12 ng/mL and 2030 ng/mL, respectively.

End point type	Primary

End point timeframe:

Days 1, 2, 3, 8, and 9

Notes:

[6] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Statistical analyses were not conducted.

End point values	Total			
Subject group type	Subject analysis set			
Number of subjects analysed	64			
Units: µg/mL				
geometric mean (geometric coefficient of variation)				
Day 1 (200 mg): N=47	0.553 (± 61)			
Day 2 (400 mg): N=47	0.985 (± 64)			
Day 3 (400 mg): N=29	1.25 (± 60)			
Day 8 (400 mg): N=64	1.48 (± 80)			
Day 9 (400 mg): N=28	1.24 (± 69)			

Statistical analyses

No statistical analyses for this end point

Primary: Time to Maximum Observed Plasma Concentration (Tmax) of Venetoclax

End point title	Time to Maximum Observed Plasma Concentration (Tmax) of Venetoclax[7]

End point description:

End point type	Primary

End point timeframe:

Days 1, 2, 3, 8, and 9

Notes:

[7] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Statistical analyses were not conducted.

End point values	Total			
Subject group type	Subject analysis set			
Number of subjects analysed	64			
Units: hours				
median (full range (min-max))				
Day 1 (200 mg): N=47	6.0 (4.0 to 24.0)			
Day 2 (400 mg): N=47	6.0 (4.0 to 24.0)			
Day 3 (400 mg): N=29	8.0 (4.0 to 9.8)			
Day 8 (400 mg): N=64	6.0 (2.3 to 24.0)			
Day 9 (400 mg): N=28	6.0 (3.7 to 8.0)			

Statistical analyses

No statistical analyses for this end point

Primary: Area Under the Plasma Concentration-time Curve from Time Zero to 8

Hours (AUC8) of Venetoclax

End point title	Area Under the Plasma Concentration-time Curve from Time Zero to 8 Hours (AUC8) of Venetoclax[8]

End point description:

End point type	Primary

End point timeframe:

Days 1, 2, 3, 8, and 9

Notes:

[8] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Statistical analyses were not conducted.

End point values	Total			
Subject group type	Subject analysis set			
Number of subjects analysed	64			
Units: µg*h/mL				
geometric mean (geometric coefficient of variation)				
Day 1 (200 mg): N=47	2.27 (± 69)			
Day 2 (400 mg): N=47	4.51 (± 60)			
Day 3 (400 mg): N=28	6.24 (± 64)			
Day 8 (400 mg): N=64	8.07 (± 81)			
Day 9 (400 mg): N=28	6.47 (± 78)			

Statistical analyses

No statistical analyses for this end point

Primary: Area Under the Plasma Concentration-time Curve from Time Zero to 24 Hours (AUC24) for Venetoclax

End point title	Area Under the Plasma Concentration-time Curve from Time Zero to 24 Hours (AUC24) for Venetoclax[9]

End point description:

End point type	Primary

End point timeframe:

Days 1, 2, and 8

Notes:

[9] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Statistical analyses were not conducted.

End point values	Total			
Subject group type	Subject analysis set			
Number of subjects analysed	64			
Units: µg*h/mL				
geometric mean (geometric coefficient of variation)				
Day 1 (200 mg): N=47	7.14 (± 65)			

Day 2 (400 mg): N=29 Day 8 (400mg): N=64	15.1 (± 65) 22.7 (± 84)			

Statistical analyses

No statistical analyses for this end point

Primary: Maximum Observed Plasma Concentration (Cmax) of Navitoclax

End point title	Maximum Observed Plasma Concentration (Cmax) of Navitoclax[10][11]

End point description:

Plasma concentrations of navitoclax were determined using a validated liquid/liquid extraction followed by high performance liquid chromatography with tandem mass spectrometric detection. The LLOQ and ULOQ for navitoclax were established at 5.07 ng/mL and 5070 ng/mL, respectively.

End point type	Primary

End point timeframe:

Days 3, 8, and 9

Notes:

[10] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Statistical analyses were not conducted.

[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: Safety Expansion subjects are included in the Navitoclax 50 mg group for PK results

End point values	Venetoclax + Navitoclax 25 mg	Venetoclax + Navitoclax 50 mg	Venetoclax + Navitoclax 100 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	16	8[12]	18	
Units: µg/mL				
geometric mean (geometric coefficient of variation)				
Day 3 (N = 14, 8, 6)	0.192 (± 60)	0.650 (± 17)	0.973 (± 49)	
Day 8 (N = 16, 31, 18)	0.326 (± 63)	1.09 (± 76)	1.50 (± 69)	
Day 9 (N = 16, 8, 4)	0.307 (± 63)	0.818 (± 57)	1.18 (± 47)	

Notes:

[12] - Day 8 also includes subjects in the Safety Expansion cohort who received 50 mg navitoclax (N=31)

Statistical analyses

No statistical analyses for this end point

Primary: Time to Maximum Observed Plasma Concentration (Tmax) of Navitoclax

End point title	Time to Maximum Observed Plasma Concentration (Tmax) of Navitoclax[13][14]

End point description:

End point type	Primary

End point timeframe:

Days 3, 8, and 9

Notes:

[13] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Statistical analyses were not conducted.

[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: Safety Expansion subjects are included in the Navitoclax 50 mg group for PK results

End point values	Venetoclax + Navitoclax 25 mg	Venetoclax + Navitoclax 50 mg	Venetoclax + Navitoclax 100 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	16	8[15]	18	
Units: hours				
median (full range (min-max))				
Day 3 (N = 14, 8, 6)	6.0 (4.0 to 9.8)	6.0 (4.0 to 8.0)	7.0 (4.0 to 8.0)	
Day 8 (N = 16, 31, 18)	7.3 (3.4 to 8.0)	6.0 (1.8 to 8.0)	6.0 (4.0 to 24.0)	
Day 9 (N = 16, 8, 4)	6.3 (0 to 8.0)	6.0 (4.0 to 8.0)	7.0 (6.0 to 8.0)	

Notes:

[15] - Day 8 also includes subjects in the Safety Expansion cohort who received 50 mg navitoclax (N=31)

Statistical analyses

No statistical analyses for this end point

Primary: Area Under the Plasma Concentration-time Curve from Time Zero to 8 Hours (AUC8) of Navitoclax

End point title	Area Under the Plasma Concentration-time Curve from Time Zero to 8 Hours (AUC8) of Navitoclax[16][17]

End point description:

End point type	Primary

End point timeframe:

Days 3, 8, and 9

Notes:

[16] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Statistical analyses were not conducted.

[17] - 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: Safety Expansion subjects are included in the Navitoclax 50 mg group for PK results

End point values	Venetoclax + Navitoclax 25 mg	Venetoclax + Navitoclax 50 mg	Venetoclax + Navitoclax 100 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	16	8[18]	18	
Units: µg*h/mL				
geometric mean (geometric coefficient of variation)				
Day 3 (N = 11, 8, 6)	0.991 (± 58)	2.65 (± 24)	3.65 (± 46)	

Day 8 (N = 16, 31, 18)	1.74 (± 54)	6.07 (± 81)	8.55 (± 66)	
Day 9 (N = 14, 8, 4)	1.79 (± 65)	4.31 (± 57)	5.86 (± 43)	

Notes:

[18] - Day 8 also includes subjects in the Safety Expansion cohort who received 50 mg navitoclax (N=31)

Statistical analyses

No statistical analyses for this end point

Primary: Area Under the Plasma Concentration-time Curve from Time Zero to 24 Hours (AUC24) for Navitoclax

End point title	Area Under the Plasma Concentration-time Curve from Time Zero to 24 Hours (AUC24) for Navitoclax[19][20]

End point description:

End point type	Primary

End point timeframe:

Day 8

Notes:

[19] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Statistical analyses were not conducted.

[20] - 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: Safety Expansion subjects are included in the Navitoclax 50 mg group for PK results

End point values	Venetoclax + Navitoclax 25 mg	Venetoclax + Navitoclax 50 mg	Venetoclax + Navitoclax 100 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	16	8[21]	18	
Units: µg*h/mL				
geometric mean (geometric coefficient of variation)	5.16 (± 59)	16.4 (± 82)	22.5 (± 62)	

Notes:

[21] - Day 8 also includes 22 subjects in the Safety Expansion cohort who received 50 mg navitoclax (N=30)

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Response Rate (ORR)

End point title	Overall Response Rate (ORR)

End point description:

Overall response rate was defined as the percentage of participants with a complete response (CR), complete remission/response with incomplete marrow recovery (CRi) or complete response without platelet recovery (CRp) for subjects with acute lymphoblastic leukemia (ALL) and CR or partial response (PR) for subjects with lymphoblastic lymphoma (LL).

End point type	Secondary

End point timeframe:

Up to the end of the study; median time on study was 19.1 months.

End point values	Venetoclax + Navitoclax 25 mg	Venetoclax + Navitoclax 50 mg	Venetoclax + Navitoclax 100 mg	Safety Expansion
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	16	11	19	22
Units: percentage of participants				
number (confidence interval 95%)	81.3 (54.4 to 96.0)	81.8 (48.2 to 97.7)	47.4 (24.4 to 71.1)	68.2 (45.1 to 86.1)

End point values	Pediatric	Adult	B-ALL	T-ALL
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	18	51	36	27
Units: percentage of participants				
number (confidence interval 95%)	72.2 (46.5 to 90.3)	64.7 (50.1 to 77.6)	77.8 (60.8 to 89.9)	51.9 (31.9 to 71.3)

End point values	LL			
Subject group type	Subject analysis set			
Number of subjects analysed	6			
Units: percentage of participants				
number (confidence interval 95%)	66.7 (22.3 to 95.7)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with a Complete Response

End point title	Percentage of Participants with a Complete Response

End point description:

The overall CR rate including CR, CRi, and CRp.

End point type	Secondary

End point timeframe:

Up to the end of the study; median time on study was 19.1. months.

End point values	Venetoclax + Navitoclax 25 mg	Venetoclax + Navitoclax 50 mg	Venetoclax + Navitoclax 100 mg	Safety Expansion
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	16	11	19	22
Units: percentage of participants				
number (confidence interval 95%)	75.0 (47.6 to 92.7)	72.7 (39.0 to 94.0)	42.1 (20.3 to 66.5)	50.0 (28.2 to 71.8)

End point values	Pediatric	Adult	B-ALL	T-ALL
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	18	51	36	27
Units: percentage of participants				
number (confidence interval 95%)	55.6 (30.8 to 78.5)	56.9 (42.2 to 70.7)	61.1 (43.5 to 76.9)	48.1 (28.7 to 68.1)

End point values	LL			
Subject group type	Subject analysis set			
Number of subjects analysed	6			
Units: percentage of participants				
number (confidence interval 95%)	66.7 (22.3 to 95.7)			

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (DOR)

End point title	Duration of Response (DOR)

End point description:

Duration of response is defined as the number of days from first response (CR, CRi, CRp, or PR) until progressive disease (PD) or death, whichever occurred first. Only "responders" (i.e., subjects who achieved a CR, CRi, CRp, or PR) were included in the analysis.
Duration of response was analyzed using Kaplan-Meier (KM) methodology. Participants with no PD or death were censored at the date of their last disease assessment. "99999" indicates values that could not be estimated.

End point type	Secondary

End point timeframe:

Median time on follow-up was 19.1 months

End point values	Venetoclax + Navitoclax 25 mg	Venetoclax + Navitoclax 50 mg	Venetoclax + Navitoclax 100 mg	Safety Expansion
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	13	9	9	15
Units: months				
median (confidence interval 95%)	9.5 (1.4 to 12.3)	8.5 (0.7 to 99999)	3.8 (0.8 to 99999)	2.1 (0.7 to 6.5)

End point values	Pediatric	Adult	B-ALL	T-ALL
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	13	33	28	14
Units: months				
median (confidence interval 95%)	3.5 (0.7 to 99999)	4.2 (2.1 to 9.1)	6.5 (1.4 to 9.5)	2.6 (1.0 to 99999)

End point values	LL			
Subject group type	Subject analysis set			
Number of subjects analysed	4			
Units: months				
median (confidence interval 95%)	2.1 (0.6 to 99999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Complete Response (DoCR)

End point title	Duration of Complete Response (DoCR)

End point description:

Duration of complete response is defined as the number of days from first complete response (CR, CRi, or CRp) until PD or death, whichever occurred first. Only "responders" (i.e., subjects who achieved a CR, CRi, or CRp) were included in the analysis.
Duration of complete response was analyzed using KM methodology. Participants with no PD or death were censored at the date of their last disease assessment. "99999" indicates values that could not be estimated.

End point type	Secondary

End point timeframe:

Median duration of follow-up was 19.1. months.

End point values	Venetoclax + Navitoclax 25 mg	Venetoclax + Navitoclax 50 mg	Venetoclax + Navitoclax 100 mg	Safety Expansion
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	12	8	8	11
Units: months				
median (confidence interval 95%)	4.2 (0.9 to 11.2)	8.8 (2.6 to 99999)	10.3 (0.8 to 99999)	2.4 (0.3 to 99999)

End point values	Pediatric	Adult	B-ALL	T-ALL
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	10	29	22	13
Units: months				
median (confidence interval 95%)	6.9 (3.5 to 99999)	6.5 (1.9 to 9.1)	7.4 (2.4 to 9.5)	3.4 (0.8 to 99999)

End point values	LL			
Subject group type	Subject analysis set			
Number of subjects analysed	4			
Units: months				
median (confidence interval 95%)	2.1 (0.3 to 99999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival

End point title	Overall Survival

End point description:

Overall survival (OS) is defined as the time from first dose until death.
OS was analyzed using KM methodology. Participants who were still alive were censored at the date of last contact. "99999" indicates values that could not be estimated.

End point type	Secondary

End point timeframe:

Median time on follow-up was 19.1 months.

End point values	Venetoclax + Navitoclax 25 mg	Venetoclax + Navitoclax 50 mg	Venetoclax + Navitoclax 100 mg	Safety Expansion
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	16	11	19	22
Units: months				
median (confidence interval 95%)	9.7 (2.7 to 15.7)	10.3 (3.3 to 99999)	4.3 (0.8 to 11.2)	5.2 (2.9 to 8.3)

End point values	Pediatric	Adult	B-ALL	T-ALL
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	18	51	36	27
Units: months				
median (confidence interval 95%)	11.4 (2.9 to 99999)	6.6 (3.3 to 8.3)	8.8 (4.0 to 11.4)	5.2 (2.9 to 7.7)

End point values	LL			
Subject group type	Subject analysis set			
Number of subjects analysed	6			
Units: months				
median (confidence interval 95%)	7.3 (2.0 to 99999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-Free Survival (PFS)

End point title	Progression-Free Survival (PFS)

End point description:

Progression-free survival was defined as the time from first dose until PD or death, whichever occurred first. PFS was analyzed using KM methodology. Participants with no PD or death were censored at the date of their last disease assessment. "99999" indicates values that could not be estimated.

End point type	Secondary

End point timeframe:

Median time on follow-up was 19.1 months.

End point values	Venetoclax + Navitoclax 25 mg	Venetoclax + Navitoclax 50 mg	Venetoclax + Navitoclax 100 mg	Safety Expansion
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	16	11	19	22
Units: months				
median (confidence interval 95%)	4.7 (1.8 to 11.7)	8.8 (1.6 to 99999)	1.9 (0.8 to 5.4)	1.7 (1.0 to 3.3)

End point values	Pediatric	Adult	B-ALL	T-ALL
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	18	51	36	27
Units: months				
median (confidence interval 95%)	1.7 (1.5 to 99999)	3.0 (1.8 to 5.4)	4.7 (1.7 to 8.8)	1.9 (1.6 to 4.7)

End point values	LL			
Subject group type	Subject analysis set			
Number of subjects analysed	6			
Units: months				
median (confidence interval 95%)	1.7 (1.5 to 99999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants Who Proceeded to Stem Cell Transplantation (SCT) or Chimeric Antigen Receptor T-cell (CAR-T) Therapy

End point title	Number of Participants Who Proceeded to Stem Cell Transplantation (SCT) or Chimeric Antigen Receptor T-cell (CAR-T) Therapy

End point description:

End point type	Secondary

End point timeframe:

Up to the end of the study; median time on study was 19.1. months.

End point values	Venetoclax + Navitoclax 25 mg	Venetoclax + Navitoclax 50 mg	Venetoclax + Navitoclax 100 mg	Safety Expansion
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	16	11	19	22
Units: participants				
SCT	2	5	1	5
CAR-T therapy	2	1	2	0

End point values	Pediatric	Adult	B-ALL	T-ALL
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	18	51	36	27
Units: participants				
SCT	5	8	7	3
CAR-T therapy	3	2	5	0

End point values	LL			
Subject group type	Subject analysis set			
Number of subjects analysed	6			
Units: participants				
SCT	3			
CAR-T therapy	0			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From first dose of study drug to 30 days after last dose; Median times on venetoclax and navitoclax were 45 days (range, 1-597) and 39 days (range, 5-595), respectively.

Adverse event reporting additional description:

One adult subject enrolled in the Venetoclax + Navitoclax 100 mg group discontinued from the study after receiving 1 dose of venetoclax and never received any navitoclax is included in the "total" column, but not the Venetoclax + Navitoclax 100 mg dose cohort.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.0

Reporting groups

Reporting group title	Venetoclax + Navitoclax 25 mg

Reporting group description:

Participants ≥ 45 kg received oral venetoclax daily, adjusted by weight, to match the exposure of the adult equivalent target doses of 200 mg on Day 1 and 400 mg on Day 2 and onwards for up to 37 weeks. From Day 3 participants also received oral navitoclax 25 mg administered daily. Participants received chemotherapy at the discretion of the Investigator.

Reporting group title	Venetoclax + Navitoclax 50 mg

Reporting group description:

Participants received oral venetoclax daily, adjusted by weight, to match the exposure of the adult equivalent target doses of 200 mg on Day 1 and 400 mg on Day 2 onwards for up to 37 weeks. From Day 3 participants also received oral navitoclax 50 mg (or 25 mg for subjects weighing < 45 kg) administered daily. Participants received chemotherapy at the discretion of the Investigator.

Reporting group title	Venetoclax + Navitoclax 100 mg

Reporting group description:

Participants received oral venetoclax daily, adjusted by weight, to match the exposure of the adult equivalent target doses of 200 mg on Day 1 and 400 mg on Day 2 onwards for up to 37 weeks. From Day 3 participants also received oral navitoclax 100 mg (50 mg for subjects weighing < 45 kg) administered daily. Participants received chemotherapy at the discretion of the Investigator.

Reporting group title	Safety Expansion

Reporting group description:

Participants received oral venetoclax, adjusted by weight to match the exposure of the adult equivalent target dose of 400 mg daily and oral navitoclax 50 mg (25 mg for subjects weighing < 45 kg) administered daily for 21 days of every 28 days. Participants also received chemotherapy at the discretion of the Investigator.

Reporting group title	Total

Reporting group description:

All participants who received venetoclax, navitoclax, and chemotherapy. Includes one subject who did not receive navitoclax.

Serious adverse events	Venetoclax + Navitoclax 25 mg	Venetoclax + Navitoclax 50 mg	Venetoclax + Navitoclax 100 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	14 / 16 (87.50%)	7 / 11 (63.64%)	14 / 19 (73.68%)
number of deaths (all causes)	13	7	14
number of deaths resulting from adverse events	4	0	5

General disorders and administration site conditions			
ASTHENIA			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DEATH			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
MULTIPLE ORGAN DYSFUNCTION SYNDROME			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NON-CARDIAC CHEST PAIN			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PYREXIA			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
HYPERSENSITIVITY			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
ACUTE RESPIRATORY FAILURE			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DYSPNOEA			

subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPOXIA			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PNEUMONITIS			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PULMONARY EMBOLISM			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RESPIRATORY DISTRESS			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RESPIRATORY FAILURE			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
ANXIETY			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CONFUSIONAL STATE			
subjects affected / exposed	0 / 16 (0.00%)	1 / 11 (9.09%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			

NEUTROPHIL COUNT DECREASED			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
CARDIAC ARREST			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
CARDIAC TAMPONADE			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PERICARDIAL EFFUSION			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
LETHARGY			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NEUROPATHY PERIPHERAL			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NEUROTOXICITY			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
PRESYNCOPE			
subjects affected / exposed	0 / 16 (0.00%)	1 / 11 (9.09%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

SEIZURE			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SOMNOLENCE			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SPINAL CORD COMPRESSION			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
FEBRILE NEUTROPENIA			
subjects affected / exposed	5 / 16 (31.25%)	5 / 11 (45.45%)	3 / 19 (15.79%)
occurrences causally related to treatment / all	1 / 6	4 / 6	3 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NEUTROPENIA			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PANCYTOPENIA			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
TYMPANIC MEMBRANE PERFORATION			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
ABDOMINAL PAIN			

subjects affected / exposed	1 / 16 (6.25%)	1 / 11 (9.09%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ABDOMINAL PAIN UPPER			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ANAL FISTULA			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ASCITES			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INTESTINAL ISCHAEMIA			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
NAUSEA			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NEUTROPENIC COLITIS			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PANCREATITIS			
subjects affected / exposed	0 / 16 (0.00%)	1 / 11 (9.09%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PANCREATITIS ACUTE			

subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RECTAL PERFORATION			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
UPPER GASTROINTESTINAL HAEMORRHAGE			
subjects affected / exposed	0 / 16 (0.00%)	1 / 11 (9.09%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VOMITING			
subjects affected / exposed	1 / 16 (6.25%)	1 / 11 (9.09%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 2	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
CHOLECYSTITIS			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CHRONIC HEPATITIS			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DRUG-INDUCED LIVER INJURY			
subjects affected / exposed	0 / 16 (0.00%)	1 / 11 (9.09%)	0 / 19 (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
HEPATIC PAIN			
subjects affected / exposed	0 / 16 (0.00%)	1 / 11 (9.09%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HEPATIC STEATOSIS			

subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
ACUTE KIDNEY INJURY			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
MYALGIA			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
BACTERAEMIA			
subjects affected / exposed	0 / 16 (0.00%)	1 / 11 (9.09%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CATHETER BACTERAEMIA			
subjects affected / exposed	0 / 16 (0.00%)	1 / 11 (9.09%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CELLULITIS			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ESCHERICHIA SEPSIS			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INFLUENZA			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

KLEBSIELLA SEPSIS			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MASTOIDITIS			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MYRINGITIS			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NEUTROPENIC SEPSIS			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PARAINFLUENZAE VIRUS INFECTION			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PNEUMONIA			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	2 / 19 (10.53%)
occurrences causally related to treatment / all	0 / 2	0 / 0	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PNEUMONIA PSEUDOMONAL			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PSEUDOMONAL SEPSIS			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SEPSIS			

subjects affected / exposed	3 / 16 (18.75%)	1 / 11 (9.09%)	3 / 19 (15.79%)
occurrences causally related to treatment / all	0 / 4	0 / 1	1 / 4
deaths causally related to treatment / all	0 / 2	0 / 0	0 / 1
SEPTIC SHOCK			
subjects affected / exposed	2 / 16 (12.50%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 2	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
SKIN INFECTION			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
STREPTOCOCCAL INFECTION			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	2 / 19 (10.53%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
URINARY TRACT INFECTION			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VARICELLA ZOSTER PNEUMONIA			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VASCULAR DEVICE INFECTION			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	2 / 19 (10.53%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VULVITIS			

subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
DEHYDRATION			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DIABETIC KETOACIDOSIS			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPERGLYCAEMIA			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPOKALAEMIA			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MALNUTRITION			
subjects affected / exposed	0 / 16 (0.00%)	1 / 11 (9.09%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
METABOLIC ACIDOSIS			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Safety Expansion	Total	
Total subjects affected by serious adverse events			
subjects affected / exposed	16 / 22 (72.73%)	52 / 69 (75.36%)	
number of deaths (all causes)	15	49	
number of deaths resulting from adverse events	1	10	

General disorders and administration site conditions			
ASTHENIA			
subjects affected / exposed	1 / 22 (4.55%)	1 / 69 (1.45%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
DEATH			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
MULTIPLE ORGAN DYSFUNCTION SYNDROME			
subjects affected / exposed	1 / 22 (4.55%)	2 / 69 (2.90%)	
occurrences causally related to treatment / all	2 / 2	2 / 3	
deaths causally related to treatment / all	1 / 1	1 / 1	
NON-CARDIAC CHEST PAIN			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
PYREXIA			
subjects affected / exposed	1 / 22 (4.55%)	3 / 69 (4.35%)	
occurrences causally related to treatment / all	0 / 1	1 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
HYPERSENSITIVITY			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
ACUTE RESPIRATORY FAILURE			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
DYSPNOEA			

subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
HYPOXIA			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
PNEUMONITIS			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
PULMONARY EMBOLISM			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
RESPIRATORY DISTRESS			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
RESPIRATORY FAILURE			
subjects affected / exposed	1 / 22 (4.55%)	2 / 69 (2.90%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
ANXIETY			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
CONFUSIONAL STATE			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			

NEUTROPHIL COUNT DECREASED			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
CARDIAC ARREST			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
CARDIAC TAMPONADE			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
PERICARDIAL EFFUSION			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
LETHARGY			
subjects affected / exposed	1 / 22 (4.55%)	1 / 69 (1.45%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
NEUROPATHY PERIPHERAL			
subjects affected / exposed	1 / 22 (4.55%)	1 / 69 (1.45%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
NEUROTOXICITY			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
PRESYNCOPE			
subjects affected / exposed	0 / 22 (0.00%)	2 / 69 (2.90%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

SEIZURE			
subjects affected / exposed	1 / 22 (4.55%)	2 / 69 (2.90%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
SOMNOLENCE			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
SPINAL CORD COMPRESSION			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
FEBRILE NEUTROPENIA			
subjects affected / exposed	6 / 22 (27.27%)	20 / 69 (28.99%)	
occurrences causally related to treatment / all	5 / 6	13 / 23	
deaths causally related to treatment / all	0 / 0	0 / 0	
NEUTROPENIA			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
PANCYTOPENIA			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
TYMPANIC MEMBRANE PERFORATION			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
ABDOMINAL PAIN			

subjects affected / exposed	0 / 22 (0.00%)	2 / 69 (2.90%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
ABDOMINAL PAIN UPPER			
subjects affected / exposed	0 / 22 (0.00%)	2 / 69 (2.90%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
ANAL FISTULA			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
ASCITES			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
INTESTINAL ISCHAEMIA			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
NAUSEA			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
NEUTROPENIC COLITIS			
subjects affected / exposed	1 / 22 (4.55%)	1 / 69 (1.45%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
PANCREATITIS			
subjects affected / exposed	1 / 22 (4.55%)	3 / 69 (4.35%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
PANCREATITIS ACUTE			

subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
RECTAL PERFORATION			
subjects affected / exposed	1 / 22 (4.55%)	1 / 69 (1.45%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
UPPER GASTROINTESTINAL HAEMORRHAGE			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
VOMITING			
subjects affected / exposed	0 / 22 (0.00%)	2 / 69 (2.90%)	
occurrences causally related to treatment / all	0 / 0	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
CHOLECYSTITIS			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
CHRONIC HEPATITIS			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
DRUG-INDUCED LIVER INJURY			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
HEPATIC PAIN			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
HEPATIC STEATOSIS			

subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
ACUTE KIDNEY INJURY			
subjects affected / exposed	1 / 22 (4.55%)	1 / 69 (1.45%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
MYALGIA			
subjects affected / exposed	1 / 22 (4.55%)	1 / 69 (1.45%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
BACTERAEMIA			
subjects affected / exposed	1 / 22 (4.55%)	3 / 69 (4.35%)	
occurrences causally related to treatment / all	1 / 1	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
CATHETER BACTERAEMIA			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
CELLULITIS			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
ESCHERICHIA SEPSIS			
subjects affected / exposed	1 / 22 (4.55%)	1 / 69 (1.45%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
INFLUENZA			
subjects affected / exposed	1 / 22 (4.55%)	1 / 69 (1.45%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

KLEBSIELLA SEPSIS			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
MASTOIDITIS			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
MYRINGITIS			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
NEUTROPENIC SEPSIS			
subjects affected / exposed	3 / 22 (13.64%)	3 / 69 (4.35%)	
occurrences causally related to treatment / all	3 / 3	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
PARAINFLUENZAE VIRUS INFECTION			
subjects affected / exposed	1 / 22 (4.55%)	1 / 69 (1.45%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
PNEUMONIA			
subjects affected / exposed	3 / 22 (13.64%)	6 / 69 (8.70%)	
occurrences causally related to treatment / all	2 / 6	3 / 11	
deaths causally related to treatment / all	0 / 1	0 / 1	
PNEUMONIA PSEUDOMONAL			
subjects affected / exposed	1 / 22 (4.55%)	1 / 69 (1.45%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
PSEUDOMONAL SEPSIS			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
SEPSIS			

subjects affected / exposed	3 / 22 (13.64%)	10 / 69 (14.49%)	
occurrences causally related to treatment / all	2 / 3	3 / 12	
deaths causally related to treatment / all	0 / 0	0 / 3	
SEPTIC SHOCK			
subjects affected / exposed	3 / 22 (13.64%)	6 / 69 (8.70%)	
occurrences causally related to treatment / all	1 / 3	2 / 7	
deaths causally related to treatment / all	0 / 0	0 / 2	
SKIN INFECTION			
subjects affected / exposed	1 / 22 (4.55%)	2 / 69 (2.90%)	
occurrences causally related to treatment / all	1 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
STREPTOCOCCAL INFECTION			
subjects affected / exposed	1 / 22 (4.55%)	1 / 69 (1.45%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	2 / 22 (9.09%)	5 / 69 (7.25%)	
occurrences causally related to treatment / all	1 / 2	2 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
URINARY TRACT INFECTION			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
VARICELLA ZOSTER PNEUMONIA			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
VASCULAR DEVICE INFECTION			
subjects affected / exposed	1 / 22 (4.55%)	3 / 69 (4.35%)	
occurrences causally related to treatment / all	1 / 1	2 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
VULVITIS			

subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
DEHYDRATION			
subjects affected / exposed	1 / 22 (4.55%)	1 / 69 (1.45%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
DIABETIC KETOACIDOSIS			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
HYPERGLYCAEMIA			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
HYPOKALAEMIA			
subjects affected / exposed	1 / 22 (4.55%)	1 / 69 (1.45%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
MALNUTRITION			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
METABOLIC ACIDOSIS			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Venetoclax + Navitoclax 25 mg	Venetoclax + Navitoclax 50 mg	Venetoclax + Navitoclax 100 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	16 / 16 (100.00%)	11 / 11 (100.00%)	19 / 19 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
OSTEOCHONDROMA			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Vascular disorders			
BRACHIOCEPHALIC VEIN THROMBOSIS			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
DEEP VEIN THROMBOSIS			
subjects affected / exposed	2 / 16 (12.50%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	2	0	0
FLUSHING			
subjects affected / exposed	1 / 16 (6.25%)	2 / 11 (18.18%)	2 / 19 (10.53%)
occurrences (all)	1	2	2
HOT FLUSH			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
HYPERTENSION			
subjects affected / exposed	3 / 16 (18.75%)	2 / 11 (18.18%)	3 / 19 (15.79%)
occurrences (all)	4	2	4
HYPOTENSION			
subjects affected / exposed	2 / 16 (12.50%)	1 / 11 (9.09%)	3 / 19 (15.79%)
occurrences (all)	2	1	3
JUGULAR VEIN THROMBOSIS			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	2	0	0
SUBCLAVIAN VEIN THROMBOSIS			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
THROMBOPHLEBITIS SUPERFICIAL			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
VENOUS THROMBOSIS LIMB			

subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
General disorders and administration site conditions			
ASTHENIA			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
CATHETER SITE PAIN			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	2
CHEST PAIN			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
CHILLS			
subjects affected / exposed	0 / 16 (0.00%)	2 / 11 (18.18%)	2 / 19 (10.53%)
occurrences (all)	0	3	2
FACE OEDEMA			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
FACIAL PAIN			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
FATIGUE			
subjects affected / exposed	2 / 16 (12.50%)	5 / 11 (45.45%)	6 / 19 (31.58%)
occurrences (all)	2	5	7
FEELING HOT			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
GAIT DISTURBANCE			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
GENERALISED OEDEMA			
subjects affected / exposed	2 / 16 (12.50%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	6	0	0
INJECTION SITE BRUISING			

subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
MALAISE			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
MEDICAL DEVICE PAIN			
subjects affected / exposed	0 / 16 (0.00%)	1 / 11 (9.09%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
MUCOSAL INFLAMMATION			
subjects affected / exposed	0 / 16 (0.00%)	1 / 11 (9.09%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
NON-CARDIAC CHEST PAIN			
subjects affected / exposed	4 / 16 (25.00%)	1 / 11 (9.09%)	0 / 19 (0.00%)
occurrences (all)	4	1	0
OEDEMA			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	2 / 19 (10.53%)
occurrences (all)	0	0	2
OEDEMA PERIPHERAL			
subjects affected / exposed	2 / 16 (12.50%)	3 / 11 (27.27%)	6 / 19 (31.58%)
occurrences (all)	2	3	6
PAIN			
subjects affected / exposed	2 / 16 (12.50%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences (all)	3	0	1
PERIPHERAL SWELLING			
subjects affected / exposed	1 / 16 (6.25%)	1 / 11 (9.09%)	1 / 19 (5.26%)
occurrences (all)	1	1	1
PYREXIA			
subjects affected / exposed	4 / 16 (25.00%)	2 / 11 (18.18%)	5 / 19 (26.32%)
occurrences (all)	6	2	6
SWELLING			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
SWELLING FACE			
subjects affected / exposed	2 / 16 (12.50%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	2	0	0
UNEVALUABLE EVENT			

subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
WITHDRAWAL SYNDROME			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Reproductive system and breast disorders			
ERECTILE DYSFUNCTION			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
GENITAL PAIN			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
OEDEMA GENITAL			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	2 / 19 (10.53%)
occurrences (all)	0	0	2
PENILE PAIN			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
SCROTAL OEDEMA			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
VAGINAL HAEMORRHAGE			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			
ASPIRATION			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
ATELECTASIS			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
COUGH			
subjects affected / exposed	1 / 16 (6.25%)	2 / 11 (18.18%)	1 / 19 (5.26%)
occurrences (all)	1	2	1
DRY THROAT			

subjects affected / exposed	0 / 16 (0.00%)	1 / 11 (9.09%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
DYSPNOEA			
subjects affected / exposed	3 / 16 (18.75%)	1 / 11 (9.09%)	2 / 19 (10.53%)
occurrences (all)	3	1	2
EPISTAXIS			
subjects affected / exposed	6 / 16 (37.50%)	2 / 11 (18.18%)	0 / 19 (0.00%)
occurrences (all)	6	2	0
HICCUPS			
subjects affected / exposed	2 / 16 (12.50%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences (all)	2	0	1
HYPOXIA			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
INCREASED UPPER AIRWAY SECRETION			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
LUNG INFILTRATION			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
MEDIASTINAL MASS			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
NASAL CONGESTION			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
OROPHARYNGEAL PAIN			
subjects affected / exposed	2 / 16 (12.50%)	1 / 11 (9.09%)	3 / 19 (15.79%)
occurrences (all)	2	1	4
PLEURAL EFFUSION			
subjects affected / exposed	4 / 16 (25.00%)	0 / 11 (0.00%)	2 / 19 (10.53%)
occurrences (all)	4	0	2
PLEURITIC PAIN			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0

PNEUMOMEDIASTINUM			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
PRODUCTIVE COUGH			
subjects affected / exposed	2 / 16 (12.50%)	0 / 11 (0.00%)	2 / 19 (10.53%)
occurrences (all)	2	0	3
PULMONARY EMBOLISM			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
PULMONARY MASS			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
PULMONARY OEDEMA			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	4 / 19 (21.05%)
occurrences (all)	1	0	4
RESPIRATORY DISTRESS			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
RESPIRATORY FAILURE			
subjects affected / exposed	3 / 16 (18.75%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences (all)	3	0	1
RESPIRATORY TRACT HAEMORRHAGE			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
RHINORRHOEA			
subjects affected / exposed	1 / 16 (6.25%)	1 / 11 (9.09%)	0 / 19 (0.00%)
occurrences (all)	1	1	0
SINUS CONGESTION			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
TACHYPNOEA			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
WHEEZING			

subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	3 / 19 (15.79%)
occurrences (all)	1	0	3
Psychiatric disorders			
ADJUSTMENT DISORDER			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
AFFECT LABILITY			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
AGITATION			
subjects affected / exposed	0 / 16 (0.00%)	1 / 11 (9.09%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
ANXIETY			
subjects affected / exposed	4 / 16 (25.00%)	2 / 11 (18.18%)	2 / 19 (10.53%)
occurrences (all)	4	2	2
CONFUSIONAL STATE			
subjects affected / exposed	2 / 16 (12.50%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences (all)	3	0	1
DELIRIUM			
subjects affected / exposed	1 / 16 (6.25%)	1 / 11 (9.09%)	0 / 19 (0.00%)
occurrences (all)	2	1	0
DEPRESSED MOOD			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
DEPRESSION			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
DYSPHORIA			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
HALLUCINATION			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
INSOMNIA			
subjects affected / exposed	7 / 16 (43.75%)	2 / 11 (18.18%)	3 / 19 (15.79%)
occurrences (all)	7	2	5

MENTAL STATUS CHANGES			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	2 / 19 (10.53%)
occurrences (all)	0	0	2
RESTLESSNESS			
subjects affected / exposed	0 / 16 (0.00%)	1 / 11 (9.09%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Investigations			
ACTIVATED PARTIAL THROMBOPLASTIN TIME PROLONGED			
subjects affected / exposed	1 / 16 (6.25%)	1 / 11 (9.09%)	2 / 19 (10.53%)
occurrences (all)	3	1	3
AEROMONAS TEST POSITIVE			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
ALANINE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	6 / 16 (37.50%)	4 / 11 (36.36%)	4 / 19 (21.05%)
occurrences (all)	12	6	6
AMMONIA INCREASED			
subjects affected / exposed	0 / 16 (0.00%)	1 / 11 (9.09%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
AMYLASE INCREASED			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	2 / 19 (10.53%)
occurrences (all)	0	0	2
ANTITHROMBIN III DECREASED			
subjects affected / exposed	0 / 16 (0.00%)	1 / 11 (9.09%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
ASPARTATE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	4 / 16 (25.00%)	1 / 11 (9.09%)	4 / 19 (21.05%)
occurrences (all)	8	1	5
BACTERIAL TEST POSITIVE			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
BLOOD ALKALINE PHOSPHATASE INCREASED			
subjects affected / exposed	3 / 16 (18.75%)	0 / 11 (0.00%)	2 / 19 (10.53%)
occurrences (all)	4	0	4

BLOOD BILIRUBIN INCREASED			
subjects affected / exposed	2 / 16 (12.50%)	3 / 11 (27.27%)	5 / 19 (26.32%)
occurrences (all)	2	4	10
BLOOD CREATININE INCREASED			
subjects affected / exposed	2 / 16 (12.50%)	0 / 11 (0.00%)	2 / 19 (10.53%)
occurrences (all)	2	0	3
BLOOD FIBRINOGEN DECREASED			
subjects affected / exposed	1 / 16 (6.25%)	1 / 11 (9.09%)	1 / 19 (5.26%)
occurrences (all)	3	1	2
BLOOD LACTIC ACID INCREASED			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
BLOOD PHOSPHORUS INCREASED			
subjects affected / exposed	0 / 16 (0.00%)	1 / 11 (9.09%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
BLOOD UREA INCREASED			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
BLOOD URIC ACID INCREASED			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
ELECTROCARDIOGRAM QT PROLONGED			
subjects affected / exposed	2 / 16 (12.50%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	2	0	0
ELECTROCARDIOGRAM T WAVE ABNORMAL			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
GAMMA-GLUTAMYLTRANSFERASE INCREASED			
subjects affected / exposed	1 / 16 (6.25%)	1 / 11 (9.09%)	0 / 19 (0.00%)
occurrences (all)	1	2	0
INTERNATIONAL NORMALISED RATIO INCREASED			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
LIPASE INCREASED			

subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
LIVER FUNCTION TEST INCREASED			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	2	0	0
LYMPHOCYTE COUNT DECREASED			
subjects affected / exposed	0 / 16 (0.00%)	1 / 11 (9.09%)	2 / 19 (10.53%)
occurrences (all)	0	4	4
LYMPHOCYTE COUNT INCREASED			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	4
NEUTROPHIL COUNT DECREASED			
subjects affected / exposed	1 / 16 (6.25%)	1 / 11 (9.09%)	1 / 19 (5.26%)
occurrences (all)	2	3	3
PLATELET COUNT DECREASED			
subjects affected / exposed	0 / 16 (0.00%)	1 / 11 (9.09%)	4 / 19 (21.05%)
occurrences (all)	0	3	9
PROTHROMBIN TIME PROLONGED			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
TRANSAMINASES INCREASED			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
URINARY SEDIMENT PRESENT			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
VITAMIN D DECREASED			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
WEIGHT DECREASED			
subjects affected / exposed	3 / 16 (18.75%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences (all)	5	0	2
WHITE BLOOD CELL COUNT DECREASED			
subjects affected / exposed	0 / 16 (0.00%)	1 / 11 (9.09%)	2 / 19 (10.53%)
occurrences (all)	0	1	4

Injury, poisoning and procedural complications			
AGITATION POSTOPERATIVE			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
CONTUSION			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	2 / 19 (10.53%)
occurrences (all)	1	0	2
FALL			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	2 / 19 (10.53%)
occurrences (all)	0	0	2
INFUSION RELATED REACTION			
subjects affected / exposed	2 / 16 (12.50%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences (all)	2	0	1
PROCEDURAL PAIN			
subjects affected / exposed	1 / 16 (6.25%)	1 / 11 (9.09%)	0 / 19 (0.00%)
occurrences (all)	1	1	0
TRANSFUSION REACTION			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
VASCULAR ACCESS COMPLICATION			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Congenital, familial and genetic disorders			
ANTITHROMBIN III DEFICIENCY			
subjects affected / exposed	1 / 16 (6.25%)	1 / 11 (9.09%)	1 / 19 (5.26%)
occurrences (all)	1	1	1
Cardiac disorders			
ATRIAL FIBRILLATION			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
BRADYCARDIA			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
LEFT VENTRICULAR DYSFUNCTION			
subjects affected / exposed	0 / 16 (0.00%)	1 / 11 (9.09%)	1 / 19 (5.26%)
occurrences (all)	0	1	1

SINUS TACHYCARDIA			
subjects affected / exposed	4 / 16 (25.00%)	2 / 11 (18.18%)	4 / 19 (21.05%)
occurrences (all)	4	2	5
SUPRAVENTRICULAR TACHYCARDIA			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
TACHYCARDIA			
subjects affected / exposed	2 / 16 (12.50%)	1 / 11 (9.09%)	3 / 19 (15.79%)
occurrences (all)	2	1	3
VENTRICULAR EXTRASYSTOLES			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	2 / 19 (10.53%)
occurrences (all)	0	0	2
Nervous system disorders			
ALTERED STATE OF CONSCIOUSNESS			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
BALANCE DISORDER			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
BURNING SENSATION			
subjects affected / exposed	0 / 16 (0.00%)	1 / 11 (9.09%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
CLUMSINESS			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
DISTURBANCE IN ATTENTION			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
DIZZINESS			
subjects affected / exposed	4 / 16 (25.00%)	2 / 11 (18.18%)	1 / 19 (5.26%)
occurrences (all)	4	3	1
DYSGEUSIA			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	2 / 19 (10.53%)
occurrences (all)	0	0	2
EPIDURAL LIPOMATOSIS			

subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
HEADACHE			
subjects affected / exposed	4 / 16 (25.00%)	3 / 11 (27.27%)	4 / 19 (21.05%)
occurrences (all)	4	5	5
HEMIPARESIS			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
HYPERSOMNIA			
subjects affected / exposed	0 / 16 (0.00%)	1 / 11 (9.09%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
HYPOAESTHESIA			
subjects affected / exposed	0 / 16 (0.00%)	2 / 11 (18.18%)	0 / 19 (0.00%)
occurrences (all)	0	2	0
LETHARGY			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
MEMORY IMPAIRMENT			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
MENTAL IMPAIRMENT			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
MYOCLONUS			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences (all)	2	0	2
NEUROPATHY PERIPHERAL			
subjects affected / exposed	4 / 16 (25.00%)	2 / 11 (18.18%)	0 / 19 (0.00%)
occurrences (all)	5	2	0
PARAESTHESIA			
subjects affected / exposed	2 / 16 (12.50%)	4 / 11 (36.36%)	1 / 19 (5.26%)
occurrences (all)	2	4	1
PERIPHERAL MOTOR NEUROPATHY			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
PERIPHERAL SENSORY NEUROPATHY			

subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	2 / 19 (10.53%)
occurrences (all)	1	0	3
SCIATICA			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
SEIZURE			
subjects affected / exposed	0 / 16 (0.00%)	1 / 11 (9.09%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
SOMNOLENCE			
subjects affected / exposed	0 / 16 (0.00%)	1 / 11 (9.09%)	1 / 19 (5.26%)
occurrences (all)	0	1	1
TREMOR			
subjects affected / exposed	0 / 16 (0.00%)	1 / 11 (9.09%)	0 / 19 (0.00%)
occurrences (all)	0	2	0
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	4 / 16 (25.00%)	3 / 11 (27.27%)	6 / 19 (31.58%)
occurrences (all)	7	6	11
BONE MARROW FAILURE			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	2	0	0
FEBRILE NEUTROPENIA			
subjects affected / exposed	3 / 16 (18.75%)	2 / 11 (18.18%)	4 / 19 (21.05%)
occurrences (all)	3	2	5
HYPOFIBRINOGENAEMIA			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
INCREASED TENDENCY TO BRUISE			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	2	0	0
LEUKOPENIA			
subjects affected / exposed	3 / 16 (18.75%)	2 / 11 (18.18%)	3 / 19 (15.79%)
occurrences (all)	11	6	8
LYMPHADENOPATHY			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0

NEUTROPENIA			
subjects affected / exposed	6 / 16 (37.50%)	4 / 11 (36.36%)	4 / 19 (21.05%)
occurrences (all)	11	9	7
PANCYTOPENIA			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
SPLENOMEGALY			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
THROMBOCYTOPENIA			
subjects affected / exposed	4 / 16 (25.00%)	2 / 11 (18.18%)	3 / 19 (15.79%)
occurrences (all)	5	5	5
Ear and labyrinth disorders			
HYPOACUSIS			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Eye disorders			
DRY EYE			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
EYE PAIN			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
EYE PRURITUS			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
OCULAR DISCOMFORT			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
OCULAR HYPERAEMIA			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
VISION BLURRED			
subjects affected / exposed	2 / 16 (12.50%)	1 / 11 (9.09%)	0 / 19 (0.00%)
occurrences (all)	2	1	0
Gastrointestinal disorders			

ABDOMINAL DISTENSION			
subjects affected / exposed	2 / 16 (12.50%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences (all)	2	0	1
ABDOMINAL PAIN			
subjects affected / exposed	5 / 16 (31.25%)	4 / 11 (36.36%)	9 / 19 (47.37%)
occurrences (all)	6	4	11
ABDOMINAL PAIN UPPER			
subjects affected / exposed	3 / 16 (18.75%)	0 / 11 (0.00%)	2 / 19 (10.53%)
occurrences (all)	3	0	2
ABDOMINAL TENDERNESS			
subjects affected / exposed	2 / 16 (12.50%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	2	0	0
ANAL INCONTINENCE			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
ANORECTAL DISCOMFORT			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
ASCITES			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
COLITIS			
subjects affected / exposed	0 / 16 (0.00%)	1 / 11 (9.09%)	2 / 19 (10.53%)
occurrences (all)	0	1	2
CONSTIPATION			
subjects affected / exposed	4 / 16 (25.00%)	2 / 11 (18.18%)	2 / 19 (10.53%)
occurrences (all)	4	2	2
DENTAL CARIES			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
DIARRHOEA			
subjects affected / exposed	9 / 16 (56.25%)	5 / 11 (45.45%)	7 / 19 (36.84%)
occurrences (all)	14	10	8
DISCOLOURED VOMIT			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0

DRY MOUTH			
subjects affected / exposed	1 / 16 (6.25%)	1 / 11 (9.09%)	0 / 19 (0.00%)
occurrences (all)	1	1	0
DYSCHEZIA			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
DYSPEPSIA			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	2 / 19 (10.53%)
occurrences (all)	0	0	2
DYSPHAGIA			
subjects affected / exposed	3 / 16 (18.75%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences (all)	3	0	1
ENTEROCOLITIS HAEMORRHAGIC			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
FLATULENCE			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
GASTRITIS			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	2
GASTROINTESTINAL HAEMORRHAGE			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
GASTROOESOPHAGEAL REFLUX DISEASE			
subjects affected / exposed	2 / 16 (12.50%)	1 / 11 (9.09%)	2 / 19 (10.53%)
occurrences (all)	2	2	2
GINGIVAL BLEEDING			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
GINGIVAL PAIN			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
GLOSSODYNIA			

subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
HAEMATOCHEZIA			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	2 / 19 (10.53%)
occurrences (all)	1	0	2
HAEMORRHOIDS			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
HYPERAESTHESIA TEETH			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
HYPOAESTHESIA ORAL			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
ILEUS			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
INTRA-ABDOMINAL FLUID COLLECTION			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
LIP SWELLING			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
LOWER GASTROINTESTINAL HAEMORRHAGE			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
MELAENA			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
MOUTH HAEMORRHAGE			
subjects affected / exposed	2 / 16 (12.50%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	2	0	0
NAUSEA			

subjects affected / exposed	10 / 16 (62.50%)	5 / 11 (45.45%)	6 / 19 (31.58%)
occurrences (all)	13	6	9
NEUTROPENIC COLITIS			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
OESOPHAGEAL PAIN			
subjects affected / exposed	0 / 16 (0.00%)	1 / 11 (9.09%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
OESOPHAGEAL ULCER			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
ORAL DISORDER			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
ORAL MUCOSAL BLISTERING			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
ORAL MUCOSAL EXFOLIATION			
subjects affected / exposed	0 / 16 (0.00%)	1 / 11 (9.09%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
ORAL PAIN			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
PARAESTHESIA ORAL			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
PROCTALGIA			
subjects affected / exposed	0 / 16 (0.00%)	1 / 11 (9.09%)	1 / 19 (5.26%)
occurrences (all)	0	1	1
PROCTITIS			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
RECTAL HAEMORRHAGE			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
RETCHING			

subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
STOMATITIS			
subjects affected / exposed	2 / 16 (12.50%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	2	0	0
TOOTH LOSS			
subjects affected / exposed	0 / 16 (0.00%)	1 / 11 (9.09%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
TOOTHACHE			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
VOMITING			
subjects affected / exposed	6 / 16 (37.50%)	4 / 11 (36.36%)	7 / 19 (36.84%)
occurrences (all)	9	5	11
Hepatobiliary disorders			
HEPATIC LESION			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
HEPATIC STEATOSIS			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
HEPATITIS			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
HYPERBILIRUBINAEMIA			
subjects affected / exposed	3 / 16 (18.75%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	5	0	0
Skin and subcutaneous tissue disorders			
ALOPECIA			
subjects affected / exposed	1 / 16 (6.25%)	1 / 11 (9.09%)	0 / 19 (0.00%)
occurrences (all)	1	1	0
DECUBITUS ULCER			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
DERMATITIS ACNEIFORM			

subjects affected / exposed	2 / 16 (12.50%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences (all)	2	0	1
DRY SKIN			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
ECCHYMOSIS			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
ERYTHEMA			
subjects affected / exposed	1 / 16 (6.25%)	1 / 11 (9.09%)	0 / 19 (0.00%)
occurrences (all)	1	1	0
ERYTHEMA MULTIFORME			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
HIDRADENITIS			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
HYPERHIDROSIS			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
INGROWING NAIL			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
NIGHT SWEATS			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
PETECHIAE			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
PRURITUS			
subjects affected / exposed	1 / 16 (6.25%)	1 / 11 (9.09%)	1 / 19 (5.26%)
occurrences (all)	1	1	1
PURPURA			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
RASH MACULAR			

subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
RASH MACULO-PAPULAR			
subjects affected / exposed	0 / 16 (0.00%)	1 / 11 (9.09%)	2 / 19 (10.53%)
occurrences (all)	0	1	2
RASH PAPULAR			
subjects affected / exposed	0 / 16 (0.00%)	1 / 11 (9.09%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
SKIN HYPERPIGMENTATION			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
SKIN IRRITATION			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
SKIN LESION			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
SKIN MASS			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Renal and urinary disorders			
ACUTE KIDNEY INJURY			
subjects affected / exposed	2 / 16 (12.50%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	3	0	0
DYSURIA			
subjects affected / exposed	1 / 16 (6.25%)	1 / 11 (9.09%)	1 / 19 (5.26%)
occurrences (all)	1	1	2
HAEMATURIA			
subjects affected / exposed	2 / 16 (12.50%)	1 / 11 (9.09%)	0 / 19 (0.00%)
occurrences (all)	2	1	0
RENAL FAILURE			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
RENAL TUBULAR NECROSIS			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0

URINARY INCONTINENCE			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
URINARY RETENTION			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Endocrine disorders			
ADRENAL INSUFFICIENCY			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
CUSHINGOID			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
HYPERTHYROIDISM			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal and connective tissue disorders			
ARTHRALGIA			
subjects affected / exposed	5 / 16 (31.25%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences (all)	7	0	1
ARTHRITIS			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
BACK PAIN			
subjects affected / exposed	5 / 16 (31.25%)	3 / 11 (27.27%)	3 / 19 (15.79%)
occurrences (all)	5	3	3
BONE PAIN			
subjects affected / exposed	2 / 16 (12.50%)	1 / 11 (9.09%)	3 / 19 (15.79%)
occurrences (all)	2	1	3
FLANK PAIN			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
GROIN PAIN			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
LUMBAR SPINAL STENOSIS			

subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
MUSCLE SPASMS			
subjects affected / exposed	4 / 16 (25.00%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	5	0	0
MUSCULAR WEAKNESS			
subjects affected / exposed	2 / 16 (12.50%)	1 / 11 (9.09%)	3 / 19 (15.79%)
occurrences (all)	2	1	4
MUSCULOSKELETAL CHEST PAIN			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
MUSCULOSKELETAL PAIN			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
MYALGIA			
subjects affected / exposed	4 / 16 (25.00%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences (all)	4	0	1
MYOPATHY			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
NECK PAIN			
subjects affected / exposed	0 / 16 (0.00%)	1 / 11 (9.09%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
PAIN IN EXTREMITY			
subjects affected / exposed	2 / 16 (12.50%)	0 / 11 (0.00%)	4 / 19 (21.05%)
occurrences (all)	2	0	4
SPINAL PAIN			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Infections and infestations			
ADENOVIRUS INFECTION			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
BACTERAEMIA			
subjects affected / exposed	0 / 16 (0.00%)	1 / 11 (9.09%)	0 / 19 (0.00%)
occurrences (all)	0	1	0

CANDIDA INFECTION			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	2 / 19 (10.53%)
occurrences (all)	1	0	2
CELLULITIS			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
CLOSTRIDIUM DIFFICILE COLITIS			
subjects affected / exposed	2 / 16 (12.50%)	1 / 11 (9.09%)	0 / 19 (0.00%)
occurrences (all)	2	1	0
CLOSTRIDIUM DIFFICILE INFECTION			
subjects affected / exposed	2 / 16 (12.50%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences (all)	2	0	1
CYTOMEGALOVIRUS INFECTION			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
CYTOMEGALOVIRUS VIRAEMIA			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
ESCHERICHIA BACTERAEMIA			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
INCISION SITE CELLULITIS			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
INFECTION			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
MENINGITIS			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
MUCOSAL INFECTION			
subjects affected / exposed	0 / 16 (0.00%)	1 / 11 (9.09%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
NASOPHARYNGITIS			
subjects affected / exposed	0 / 16 (0.00%)	1 / 11 (9.09%)	0 / 19 (0.00%)
occurrences (all)	0	1	0

ORAL CANDIDIASIS			
subjects affected / exposed	0 / 16 (0.00%)	1 / 11 (9.09%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
OROPHARYNGEAL CANDIDIASIS			
subjects affected / exposed	0 / 16 (0.00%)	1 / 11 (9.09%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
PARONYCHIA			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
PNEUMONIA			
subjects affected / exposed	2 / 16 (12.50%)	2 / 11 (18.18%)	2 / 19 (10.53%)
occurrences (all)	2	2	2
PNEUMONIA ADENOVIRAL			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
PNEUMONIA BACTERIAL			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
PNEUMONIA FUNGAL			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
RASH PUSTULAR			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
RESPIRATORY SYNCYTIAL VIRUS INFECTION			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
RHINITIS			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
RHINOVIRUS INFECTION			
subjects affected / exposed	3 / 16 (18.75%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	3	0	0
SEPSIS			

subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
SINUSITIS			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
SKIN INFECTION			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
SOFT TISSUE INFECTION			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
STREPTOCOCCAL BACTERAEMIA			
subjects affected / exposed	0 / 16 (0.00%)	1 / 11 (9.09%)	1 / 19 (5.26%)
occurrences (all)	0	1	1
STREPTOCOCCAL INFECTION			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
SUBCUTANEOUS ABSCESS			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	1 / 16 (6.25%)	2 / 11 (18.18%)	1 / 19 (5.26%)
occurrences (all)	1	2	1
URINARY TRACT INFECTION			
subjects affected / exposed	0 / 16 (0.00%)	1 / 11 (9.09%)	1 / 19 (5.26%)
occurrences (all)	0	1	1
Metabolism and nutrition disorders			
APPETITE DISORDER			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
DECREASED APPETITE			
subjects affected / exposed	3 / 16 (18.75%)	1 / 11 (9.09%)	6 / 19 (31.58%)
occurrences (all)	3	1	8
DEHYDRATION			

subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
ELECTROLYTE IMBALANCE			
subjects affected / exposed	2 / 16 (12.50%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	2	0	0
FLUID OVERLOAD			
subjects affected / exposed	1 / 16 (6.25%)	1 / 11 (9.09%)	1 / 19 (5.26%)
occurrences (all)	1	1	1
GOUT			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
HYPERAMMONAEMIA			
subjects affected / exposed	1 / 16 (6.25%)	1 / 11 (9.09%)	0 / 19 (0.00%)
occurrences (all)	1	1	0
HYPERCALCAEMIA			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
HYPERGLYCAEMIA			
subjects affected / exposed	4 / 16 (25.00%)	2 / 11 (18.18%)	4 / 19 (21.05%)
occurrences (all)	8	2	9
HYPERKALAEMIA			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	4 / 19 (21.05%)
occurrences (all)	1	0	4
HYPERMAGNESAEMIA			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	2
HYPERNATRAEMIA			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	3
HYPERPHOSPHATAEMIA			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	2 / 19 (10.53%)
occurrences (all)	1	0	2
HYPERTRIGLYCERIDAEMIA			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences (all)	2	0	1
HYPERURICAEMIA			

subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
HYPOALBUMINAEMIA			
subjects affected / exposed	2 / 16 (12.50%)	2 / 11 (18.18%)	4 / 19 (21.05%)
occurrences (all)	4	3	6
HYPOCALCAEMIA			
subjects affected / exposed	4 / 16 (25.00%)	1 / 11 (9.09%)	7 / 19 (36.84%)
occurrences (all)	10	1	12
HYPOGLYCAEMIA			
subjects affected / exposed	1 / 16 (6.25%)	3 / 11 (27.27%)	4 / 19 (21.05%)
occurrences (all)	1	5	6
HYPOKALAEMIA			
subjects affected / exposed	7 / 16 (43.75%)	5 / 11 (45.45%)	11 / 19 (57.89%)
occurrences (all)	17	8	17
HYPOMAGNESAEMIA			
subjects affected / exposed	4 / 16 (25.00%)	2 / 11 (18.18%)	4 / 19 (21.05%)
occurrences (all)	4	2	9
HYPONATRAEMIA			
subjects affected / exposed	6 / 16 (37.50%)	2 / 11 (18.18%)	4 / 19 (21.05%)
occurrences (all)	8	3	7
HYPOPHOSPHATAEMIA			
subjects affected / exposed	1 / 16 (6.25%)	2 / 11 (18.18%)	4 / 19 (21.05%)
occurrences (all)	3	3	7
HYPOVOLAEMIA			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
INCREASED APPETITE			
subjects affected / exposed	0 / 16 (0.00%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
INSULIN RESISTANCE			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
TUMOUR LYSIS SYNDROME			
subjects affected / exposed	1 / 16 (6.25%)	0 / 11 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1

Non-serious adverse events	Safety Expansion	Total	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	22 / 22 (100.00%)	69 / 69 (100.00%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
OSTEOCHONDROMA			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
Vascular disorders			
BRACHIOCEPHALIC VEIN THROMBOSIS			
subjects affected / exposed	0 / 22 (0.00%)	2 / 69 (2.90%)	
occurrences (all)	0	2	
DEEP VEIN THROMBOSIS			
subjects affected / exposed	1 / 22 (4.55%)	3 / 69 (4.35%)	
occurrences (all)	1	3	
FLUSHING			
subjects affected / exposed	2 / 22 (9.09%)	7 / 69 (10.14%)	
occurrences (all)	2	7	
HOT FLUSH			
subjects affected / exposed	1 / 22 (4.55%)	2 / 69 (2.90%)	
occurrences (all)	1	2	
HYPERTENSION			
subjects affected / exposed	5 / 22 (22.73%)	13 / 69 (18.84%)	
occurrences (all)	5	15	
HYPOTENSION			
subjects affected / exposed	3 / 22 (13.64%)	9 / 69 (13.04%)	
occurrences (all)	4	10	
JUGULAR VEIN THROMBOSIS			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	2	
SUBCLAVIAN VEIN THROMBOSIS			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
THROMBOPHLEBITIS SUPERFICIAL			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
VENOUS THROMBOSIS LIMB			

subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
General disorders and administration site conditions			
ASTHENIA			
subjects affected / exposed	1 / 22 (4.55%)	2 / 69 (2.90%)	
occurrences (all)	1	2	
CATHETER SITE PAIN			
subjects affected / exposed	1 / 22 (4.55%)	2 / 69 (2.90%)	
occurrences (all)	1	3	
CHEST PAIN			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
CHILLS			
subjects affected / exposed	4 / 22 (18.18%)	8 / 69 (11.59%)	
occurrences (all)	4	9	
FACE OEDEMA			
subjects affected / exposed	1 / 22 (4.55%)	2 / 69 (2.90%)	
occurrences (all)	1	2	
FACIAL PAIN			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
FATIGUE			
subjects affected / exposed	11 / 22 (50.00%)	25 / 69 (36.23%)	
occurrences (all)	13	28	
FEELING HOT			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
GAIT DISTURBANCE			
subjects affected / exposed	1 / 22 (4.55%)	2 / 69 (2.90%)	
occurrences (all)	2	3	
GENERALISED OEDEMA			
subjects affected / exposed	0 / 22 (0.00%)	2 / 69 (2.90%)	
occurrences (all)	0	6	
INJECTION SITE BRUISING			

subjects affected / exposed	1 / 22 (4.55%)	2 / 69 (2.90%)	
occurrences (all)	1	2	
MALAISE			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
MEDICAL DEVICE PAIN			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
MUCOSAL INFLAMMATION			
subjects affected / exposed	2 / 22 (9.09%)	3 / 69 (4.35%)	
occurrences (all)	2	3	
NON-CARDIAC CHEST PAIN			
subjects affected / exposed	0 / 22 (0.00%)	5 / 69 (7.25%)	
occurrences (all)	0	5	
OEDEMA			
subjects affected / exposed	1 / 22 (4.55%)	3 / 69 (4.35%)	
occurrences (all)	1	3	
OEDEMA PERIPHERAL			
subjects affected / exposed	6 / 22 (27.27%)	18 / 69 (26.09%)	
occurrences (all)	10	22	
PAIN			
subjects affected / exposed	3 / 22 (13.64%)	6 / 69 (8.70%)	
occurrences (all)	3	7	
PERIPHERAL SWELLING			
subjects affected / exposed	0 / 22 (0.00%)	3 / 69 (4.35%)	
occurrences (all)	0	3	
PYREXIA			
subjects affected / exposed	2 / 22 (9.09%)	13 / 69 (18.84%)	
occurrences (all)	2	16	
SWELLING			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
SWELLING FACE			
subjects affected / exposed	0 / 22 (0.00%)	2 / 69 (2.90%)	
occurrences (all)	0	2	
UNEVALUABLE EVENT			

subjects affected / exposed	3 / 22 (13.64%)	4 / 69 (5.80%)	
occurrences (all)	3	4	
WITHDRAWAL SYNDROME			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
Reproductive system and breast disorders			
ERECTILE DYSFUNCTION			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
GENITAL PAIN			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
OEDEMA GENITAL			
subjects affected / exposed	0 / 22 (0.00%)	2 / 69 (2.90%)	
occurrences (all)	0	2	
PENILE PAIN			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
SCROTAL OEDEMA			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
VAGINAL HAEMORRHAGE			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
ASPIRATION			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
ATELECTASIS			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
COUGH			
subjects affected / exposed	5 / 22 (22.73%)	9 / 69 (13.04%)	
occurrences (all)	5	9	
DRY THROAT			

subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)		
occurrences (all)	0	1		
DYSPNOEA				
subjects affected / exposed	1 / 22 (4.55%)	7 / 69 (10.14%)		
occurrences (all)	1	7		
EPISTAXIS				
subjects affected / exposed	1 / 22 (4.55%)	9 / 69 (13.04%)		
occurrences (all)	1	9		
HICCUPS				
subjects affected / exposed	1 / 22 (4.55%)	4 / 69 (5.80%)		
occurrences (all)	1	4		
HYPOXIA				
subjects affected / exposed	1 / 22 (4.55%)	3 / 69 (4.35%)		
occurrences (all)	1	3		
INCREASED UPPER AIRWAY SECRETION				
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)		
occurrences (all)	0	1		
LUNG INFILTRATION				
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)		
occurrences (all)	0	1		
MEDIASTINAL MASS				
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)		
occurrences (all)	0	1		
NASAL CONGESTION				
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)		
occurrences (all)	0	1		
OROPHARYNGEAL PAIN				
subjects affected / exposed	1 / 22 (4.55%)	7 / 69 (10.14%)		
occurrences (all)	1	8		
PLEURAL EFFUSION				
subjects affected / exposed	1 / 22 (4.55%)	7 / 69 (10.14%)		
occurrences (all)	1	7		
PLEURITIC PAIN				
subjects affected / exposed	1 / 22 (4.55%)	2 / 69 (2.90%)		
occurrences (all)	1	2		

PNEUMOMEDIASTINUM				
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)		
occurrences (all)	0	1		
PRODUCTIVE COUGH				
subjects affected / exposed	1 / 22 (4.55%)	5 / 69 (7.25%)		
occurrences (all)	1	6		
PULMONARY EMBOLISM				
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)		
occurrences (all)	0	1		
PULMONARY MASS				
subjects affected / exposed	0 / 22 (0.00%)	2 / 69 (2.90%)		
occurrences (all)	0	2		
PULMONARY OEDEMA				
subjects affected / exposed	0 / 22 (0.00%)	5 / 69 (7.25%)		
occurrences (all)	0	5		
RESPIRATORY DISTRESS				
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)		
occurrences (all)	0	1		
RESPIRATORY FAILURE				
subjects affected / exposed	0 / 22 (0.00%)	4 / 69 (5.80%)		
occurrences (all)	0	4		
RESPIRATORY TRACT HAEMORRHAGE				
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)		
occurrences (all)	0	1		
RHINORRHOEA				
subjects affected / exposed	2 / 22 (9.09%)	4 / 69 (5.80%)		
occurrences (all)	3	5		
SINUS CONGESTION				
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)		
occurrences (all)	0	1		
TACHYPNOEA				
subjects affected / exposed	1 / 22 (4.55%)	2 / 69 (2.90%)		
occurrences (all)	1	2		
WHEEZING				

subjects affected / exposed	0 / 22 (0.00%)	4 / 69 (5.80%)	
occurrences (all)	0	4	
Psychiatric disorders			
ADJUSTMENT DISORDER			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
AFFECT LABILITY			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
AGITATION			
subjects affected / exposed	1 / 22 (4.55%)	2 / 69 (2.90%)	
occurrences (all)	1	2	
ANXIETY			
subjects affected / exposed	1 / 22 (4.55%)	9 / 69 (13.04%)	
occurrences (all)	1	9	
CONFUSIONAL STATE			
subjects affected / exposed	3 / 22 (13.64%)	6 / 69 (8.70%)	
occurrences (all)	3	7	
DELIRIUM			
subjects affected / exposed	1 / 22 (4.55%)	3 / 69 (4.35%)	
occurrences (all)	1	4	
DEPRESSED MOOD			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
DEPRESSION			
subjects affected / exposed	1 / 22 (4.55%)	3 / 69 (4.35%)	
occurrences (all)	1	3	
DYSPHORIA			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
HALLUCINATION			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
INSOMNIA			
subjects affected / exposed	6 / 22 (27.27%)	18 / 69 (26.09%)	
occurrences (all)	6	20	

MENTAL STATUS CHANGES			
subjects affected / exposed	2 / 22 (9.09%)	4 / 69 (5.80%)	
occurrences (all)	2	4	
RESTLESSNESS			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
Investigations			
ACTIVATED PARTIAL THROMBOPLASTIN TIME PROLONGED			
subjects affected / exposed	6 / 22 (27.27%)	10 / 69 (14.49%)	
occurrences (all)	7	14	
AEROMONAS TEST POSITIVE			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
ALANINE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	8 / 22 (36.36%)	22 / 69 (31.88%)	
occurrences (all)	13	37	
AMMONIA INCREASED			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
AMYLASE INCREASED			
subjects affected / exposed	2 / 22 (9.09%)	4 / 69 (5.80%)	
occurrences (all)	2	4	
ANTITHROMBIN III DECREASED			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
ASPARTATE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	9 / 22 (40.91%)	18 / 69 (26.09%)	
occurrences (all)	14	28	
BACTERIAL TEST POSITIVE			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
BLOOD ALKALINE PHOSPHATASE INCREASED			
subjects affected / exposed	4 / 22 (18.18%)	9 / 69 (13.04%)	
occurrences (all)	7	15	

BLOOD BILIRUBIN INCREASED			
subjects affected / exposed	8 / 22 (36.36%)	18 / 69 (26.09%)	
occurrences (all)	13	29	
BLOOD CREATININE INCREASED			
subjects affected / exposed	3 / 22 (13.64%)	7 / 69 (10.14%)	
occurrences (all)	4	9	
BLOOD FIBRINOGEN DECREASED			
subjects affected / exposed	3 / 22 (13.64%)	6 / 69 (8.70%)	
occurrences (all)	3	9	
BLOOD LACTIC ACID INCREASED			
subjects affected / exposed	0 / 22 (0.00%)	2 / 69 (2.90%)	
occurrences (all)	0	2	
BLOOD PHOSPHORUS INCREASED			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
BLOOD UREA INCREASED			
subjects affected / exposed	0 / 22 (0.00%)	2 / 69 (2.90%)	
occurrences (all)	0	2	
BLOOD URIC ACID INCREASED			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
ELECTROCARDIOGRAM QT PROLONGED			
subjects affected / exposed	1 / 22 (4.55%)	3 / 69 (4.35%)	
occurrences (all)	1	3	
ELECTROCARDIOGRAM T WAVE ABNORMAL			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
GAMMA-GLUTAMYLTRANSFERASE INCREASED			
subjects affected / exposed	0 / 22 (0.00%)	2 / 69 (2.90%)	
occurrences (all)	0	3	
INTERNATIONAL NORMALISED RATIO INCREASED			
subjects affected / exposed	1 / 22 (4.55%)	2 / 69 (2.90%)	
occurrences (all)	1	2	
LIPASE INCREASED			

subjects affected / exposed	3 / 22 (13.64%)	5 / 69 (7.25%)	
occurrences (all)	4	6	
LIVER FUNCTION TEST INCREASED			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	2	
LYMPHOCYTE COUNT DECREASED			
subjects affected / exposed	3 / 22 (13.64%)	6 / 69 (8.70%)	
occurrences (all)	5	13	
LYMPHOCYTE COUNT INCREASED			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	4	
NEUTROPHIL COUNT DECREASED			
subjects affected / exposed	5 / 22 (22.73%)	8 / 69 (11.59%)	
occurrences (all)	6	14	
PLATELET COUNT DECREASED			
subjects affected / exposed	4 / 22 (18.18%)	9 / 69 (13.04%)	
occurrences (all)	7	19	
PROTHROMBIN TIME PROLONGED			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
TRANSAMINASES INCREASED			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
URINARY SEDIMENT PRESENT			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
VITAMIN D DECREASED			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
WEIGHT DECREASED			
subjects affected / exposed	4 / 22 (18.18%)	8 / 69 (11.59%)	
occurrences (all)	4	11	
WHITE BLOOD CELL COUNT DECREASED			
subjects affected / exposed	3 / 22 (13.64%)	6 / 69 (8.70%)	
occurrences (all)	3	8	

Injury, poisoning and procedural complications			
AGITATION POSTOPERATIVE			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
CONTUSION			
subjects affected / exposed	2 / 22 (9.09%)	5 / 69 (7.25%)	
occurrences (all)	3	6	
FALL			
subjects affected / exposed	2 / 22 (9.09%)	4 / 69 (5.80%)	
occurrences (all)	2	4	
INFUSION RELATED REACTION			
subjects affected / exposed	1 / 22 (4.55%)	4 / 69 (5.80%)	
occurrences (all)	1	4	
PROCEDURAL PAIN			
subjects affected / exposed	0 / 22 (0.00%)	2 / 69 (2.90%)	
occurrences (all)	0	2	
TRANSFUSION REACTION			
subjects affected / exposed	0 / 22 (0.00%)	2 / 69 (2.90%)	
occurrences (all)	0	2	
VASCULAR ACCESS COMPLICATION			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
Congenital, familial and genetic disorders			
ANTITHROMBIN III DEFICIENCY			
subjects affected / exposed	3 / 22 (13.64%)	6 / 69 (8.70%)	
occurrences (all)	3	6	
Cardiac disorders			
ATRIAL FIBRILLATION			
subjects affected / exposed	0 / 22 (0.00%)	2 / 69 (2.90%)	
occurrences (all)	0	2	
BRADYCARDIA			
subjects affected / exposed	2 / 22 (9.09%)	2 / 69 (2.90%)	
occurrences (all)	2	2	
LEFT VENTRICULAR DYSFUNCTION			
subjects affected / exposed	0 / 22 (0.00%)	2 / 69 (2.90%)	
occurrences (all)	0	2	

SINUS TACHYCARDIA			
subjects affected / exposed	1 / 22 (4.55%)	11 / 69 (15.94%)	
occurrences (all)	1	12	
SUPRAVENTRICULAR TACHYCARDIA			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
TACHYCARDIA			
subjects affected / exposed	7 / 22 (31.82%)	13 / 69 (18.84%)	
occurrences (all)	8	14	
VENTRICULAR EXTRASYSTOLES			
subjects affected / exposed	1 / 22 (4.55%)	3 / 69 (4.35%)	
occurrences (all)	1	3	
Nervous system disorders			
ALTERED STATE OF CONSCIOUSNESS			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
BALANCE DISORDER			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
BURNING SENSATION			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
CLUMSINESS			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
DISTURBANCE IN ATTENTION			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
DIZZINESS			
subjects affected / exposed	1 / 22 (4.55%)	8 / 69 (11.59%)	
occurrences (all)	1	9	
DYSGEUSIA			
subjects affected / exposed	0 / 22 (0.00%)	2 / 69 (2.90%)	
occurrences (all)	0	2	
EPIDURAL LIPOMATOSIS			

subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
HEADACHE			
subjects affected / exposed	5 / 22 (22.73%)	16 / 69 (23.19%)	
occurrences (all)	5	19	
HEMIPARESIS			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
HYPERSOMNIA			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
HYPOAESTHESIA			
subjects affected / exposed	0 / 22 (0.00%)	2 / 69 (2.90%)	
occurrences (all)	0	2	
LETHARGY			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
MEMORY IMPAIRMENT			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
MENTAL IMPAIRMENT			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
MYOCLONUS			
subjects affected / exposed	0 / 22 (0.00%)	2 / 69 (2.90%)	
occurrences (all)	0	4	
NEUROPATHY PERIPHERAL			
subjects affected / exposed	2 / 22 (9.09%)	8 / 69 (11.59%)	
occurrences (all)	2	9	
PARAESTHESIA			
subjects affected / exposed	0 / 22 (0.00%)	7 / 69 (10.14%)	
occurrences (all)	0	7	
PERIPHERAL MOTOR NEUROPATHY			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
PERIPHERAL SENSORY NEUROPATHY			

subjects affected / exposed	2 / 22 (9.09%)	5 / 69 (7.25%)	
occurrences (all)	2	6	
SCIATICA			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
SEIZURE			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
SOMNOLENCE			
subjects affected / exposed	0 / 22 (0.00%)	2 / 69 (2.90%)	
occurrences (all)	0	2	
TREMOR			
subjects affected / exposed	1 / 22 (4.55%)	2 / 69 (2.90%)	
occurrences (all)	1	3	
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	10 / 22 (45.45%)	23 / 69 (33.33%)	
occurrences (all)	11	35	
BONE MARROW FAILURE			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	2	
FEBRILE NEUTROPENIA			
subjects affected / exposed	2 / 22 (9.09%)	11 / 69 (15.94%)	
occurrences (all)	2	12	
HYPOFIBRINOGENAEMIA			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
INCREASED TENDENCY TO BRUISE			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	2	
LEUKOPENIA			
subjects affected / exposed	4 / 22 (18.18%)	12 / 69 (17.39%)	
occurrences (all)	4	29	
LYMPHADENOPATHY			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	

NEUTROPENIA			
subjects affected / exposed	6 / 22 (27.27%)	20 / 69 (28.99%)	
occurrences (all)	8	35	
PANCYTOPENIA			
subjects affected / exposed	1 / 22 (4.55%)	2 / 69 (2.90%)	
occurrences (all)	1	2	
SPLENOMEGALY			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
THROMBOCYTOPENIA			
subjects affected / exposed	5 / 22 (22.73%)	14 / 69 (20.29%)	
occurrences (all)	6	21	
Ear and labyrinth disorders			
HYPOACUSIS			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
Eye disorders			
DRY EYE			
subjects affected / exposed	0 / 22 (0.00%)	2 / 69 (2.90%)	
occurrences (all)	0	2	
EYE PAIN			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
EYE PRURITUS			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
OCULAR DISCOMFORT			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
OCULAR HYPERAEMIA			
subjects affected / exposed	2 / 22 (9.09%)	2 / 69 (2.90%)	
occurrences (all)	2	2	
VISION BLURRED			
subjects affected / exposed	1 / 22 (4.55%)	4 / 69 (5.80%)	
occurrences (all)	1	4	
Gastrointestinal disorders			

ABDOMINAL DISTENSION			
subjects affected / exposed	3 / 22 (13.64%)	6 / 69 (8.70%)	
occurrences (all)	3	6	
ABDOMINAL PAIN			
subjects affected / exposed	7 / 22 (31.82%)	26 / 69 (37.68%)	
occurrences (all)	8	30	
ABDOMINAL PAIN UPPER			
subjects affected / exposed	0 / 22 (0.00%)	5 / 69 (7.25%)	
occurrences (all)	0	5	
ABDOMINAL TENDERNESS			
subjects affected / exposed	0 / 22 (0.00%)	2 / 69 (2.90%)	
occurrences (all)	0	2	
ANAL INCONTINENCE			
subjects affected / exposed	0 / 22 (0.00%)	2 / 69 (2.90%)	
occurrences (all)	0	2	
ANORECTAL DISCOMFORT			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
ASCITES			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
COLITIS			
subjects affected / exposed	2 / 22 (9.09%)	5 / 69 (7.25%)	
occurrences (all)	2	5	
CONSTIPATION			
subjects affected / exposed	9 / 22 (40.91%)	17 / 69 (24.64%)	
occurrences (all)	9	17	
DENTAL CARIES			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
DIARRHOEA			
subjects affected / exposed	13 / 22 (59.09%)	35 / 69 (50.72%)	
occurrences (all)	15	48	
DISCOLOURED VOMIT			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	

DRY MOUTH				
subjects affected / exposed	0 / 22 (0.00%)	2 / 69 (2.90%)		
occurrences (all)	0	2		
DYSCHEZIA				
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)		
occurrences (all)	0	1		
DYSPEPSIA				
subjects affected / exposed	1 / 22 (4.55%)	4 / 69 (5.80%)		
occurrences (all)	1	4		
DYSPHAGIA				
subjects affected / exposed	0 / 22 (0.00%)	4 / 69 (5.80%)		
occurrences (all)	0	4		
ENTEROCOLITIS HAEMORRHAGIC				
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)		
occurrences (all)	0	1		
FLATULENCE				
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)		
occurrences (all)	0	1		
GASTRITIS				
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)		
occurrences (all)	0	2		
GASTROINTESTINAL HAEMORRHAGE				
subjects affected / exposed	0 / 22 (0.00%)	2 / 69 (2.90%)		
occurrences (all)	0	2		
GASTROOESOPHAGEAL REFLUX DISEASE				
subjects affected / exposed	3 / 22 (13.64%)	8 / 69 (11.59%)		
occurrences (all)	3	9		
GINGIVAL BLEEDING				
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)		
occurrences (all)	0	1		
GINGIVAL PAIN				
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)		
occurrences (all)	0	1		
GLOSSODYNIA				

subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)		
occurrences (all)	0	1		
HAEMATOCHEZIA				
subjects affected / exposed	0 / 22 (0.00%)	3 / 69 (4.35%)		
occurrences (all)	0	3		
HAEMORRHOIDS				
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)		
occurrences (all)	0	1		
HYPERAESTHESIA TEETH				
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)		
occurrences (all)	0	1		
HYPOAESTHESIA ORAL				
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)		
occurrences (all)	0	1		
ILEUS				
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)		
occurrences (all)	0	1		
INTRA-ABDOMINAL FLUID COLLECTION				
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)		
occurrences (all)	0	1		
LIP SWELLING				
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)		
occurrences (all)	0	1		
LOWER GASTROINTESTINAL HAEMORRHAGE				
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)		
occurrences (all)	0	1		
MELAENA				
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)		
occurrences (all)	0	1		
MOUTH HAEMORRHAGE				
subjects affected / exposed	0 / 22 (0.00%)	2 / 69 (2.90%)		
occurrences (all)	0	2		
NAUSEA				

subjects affected / exposed	14 / 22 (63.64%)	36 / 69 (52.17%)	
occurrences (all)	17	46	
NEUTROPENIC COLITIS			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
OESOPHAGEAL PAIN			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
OESOPHAGEAL ULCER			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
ORAL DISORDER			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
ORAL MUCOSAL BLISTERING			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
ORAL MUCOSAL EXFOLIATION			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
ORAL PAIN			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
PARAESTHESIA ORAL			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
PROCTALGIA			
subjects affected / exposed	0 / 22 (0.00%)	2 / 69 (2.90%)	
occurrences (all)	0	2	
PROCTITIS			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
RECTAL HAEMORRHAGE			
subjects affected / exposed	1 / 22 (4.55%)	3 / 69 (4.35%)	
occurrences (all)	1	3	
RETCHING			

subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
STOMATITIS			
subjects affected / exposed	0 / 22 (0.00%)	3 / 69 (4.35%)	
occurrences (all)	0	3	
TOOTH LOSS			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
TOOTHACHE			
subjects affected / exposed	2 / 22 (9.09%)	3 / 69 (4.35%)	
occurrences (all)	2	3	
VOMITING			
subjects affected / exposed	9 / 22 (40.91%)	26 / 69 (37.68%)	
occurrences (all)	10	35	
Hepatobiliary disorders			
HEPATIC LESION			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
HEPATIC STEATOSIS			
subjects affected / exposed	2 / 22 (9.09%)	3 / 69 (4.35%)	
occurrences (all)	2	3	
HEPATITIS			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
HYPERBILIRUBINAEMIA			
subjects affected / exposed	3 / 22 (13.64%)	6 / 69 (8.70%)	
occurrences (all)	4	9	
Skin and subcutaneous tissue disorders			
ALOPECIA			
subjects affected / exposed	0 / 22 (0.00%)	2 / 69 (2.90%)	
occurrences (all)	0	2	
DECUBITUS ULCER			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
DERMATITIS ACNEIFORM			

subjects affected / exposed	3 / 22 (13.64%)	6 / 69 (8.70%)	
occurrences (all)	3	6	
DRY SKIN			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
ECCHYMOSIS			
subjects affected / exposed	0 / 22 (0.00%)	2 / 69 (2.90%)	
occurrences (all)	0	2	
ERYTHEMA			
subjects affected / exposed	0 / 22 (0.00%)	2 / 69 (2.90%)	
occurrences (all)	0	2	
ERYTHEMA MULTIFORME			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
HIDRADENITIS			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
HYPERHIDROSIS			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
INGROWING NAIL			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
NIGHT SWEATS			
subjects affected / exposed	1 / 22 (4.55%)	3 / 69 (4.35%)	
occurrences (all)	1	3	
PETECHIAE			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
PRURITUS			
subjects affected / exposed	1 / 22 (4.55%)	4 / 69 (5.80%)	
occurrences (all)	1	4	
PURPURA			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
RASH MACULAR			

subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
RASH MACULO-PAPULAR			
subjects affected / exposed	1 / 22 (4.55%)	4 / 69 (5.80%)	
occurrences (all)	1	4	
RASH PAPULAR			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
SKIN HYPERPIGMENTATION			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
SKIN IRRITATION			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
SKIN LESION			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
SKIN MASS			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
Renal and urinary disorders			
ACUTE KIDNEY INJURY			
subjects affected / exposed	1 / 22 (4.55%)	3 / 69 (4.35%)	
occurrences (all)	2	5	
DYSURIA			
subjects affected / exposed	0 / 22 (0.00%)	3 / 69 (4.35%)	
occurrences (all)	0	4	
HAEMATURIA			
subjects affected / exposed	2 / 22 (9.09%)	5 / 69 (7.25%)	
occurrences (all)	2	5	
RENAL FAILURE			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
RENAL TUBULAR NECROSIS			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	

URINARY INCONTINENCE			
subjects affected / exposed	0 / 22 (0.00%)	2 / 69 (2.90%)	
occurrences (all)	0	2	
URINARY RETENTION			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
Endocrine disorders			
ADRENAL INSUFFICIENCY			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
CUSHINGOID			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
HYPERTHYROIDISM			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
ARTHRALGIA			
subjects affected / exposed	2 / 22 (9.09%)	8 / 69 (11.59%)	
occurrences (all)	3	11	
ARTHRITIS			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
BACK PAIN			
subjects affected / exposed	3 / 22 (13.64%)	14 / 69 (20.29%)	
occurrences (all)	4	15	
BONE PAIN			
subjects affected / exposed	0 / 22 (0.00%)	6 / 69 (8.70%)	
occurrences (all)	0	6	
FLANK PAIN			
subjects affected / exposed	3 / 22 (13.64%)	4 / 69 (5.80%)	
occurrences (all)	3	4	
GROIN PAIN			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
LUMBAR SPINAL STENOSIS			

subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
MUSCLE SPASMS			
subjects affected / exposed	2 / 22 (9.09%)	6 / 69 (8.70%)	
occurrences (all)	2	7	
MUSCULAR WEAKNESS			
subjects affected / exposed	3 / 22 (13.64%)	9 / 69 (13.04%)	
occurrences (all)	3	10	
MUSCULOSKELETAL CHEST PAIN			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
MUSCULOSKELETAL PAIN			
subjects affected / exposed	4 / 22 (18.18%)	5 / 69 (7.25%)	
occurrences (all)	4	5	
MYALGIA			
subjects affected / exposed	0 / 22 (0.00%)	5 / 69 (7.25%)	
occurrences (all)	0	5	
MYOPATHY			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
NECK PAIN			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
PAIN IN EXTREMITY			
subjects affected / exposed	3 / 22 (13.64%)	9 / 69 (13.04%)	
occurrences (all)	3	9	
SPINAL PAIN			
subjects affected / exposed	1 / 22 (4.55%)	2 / 69 (2.90%)	
occurrences (all)	1	2	
Infections and infestations			
ADENOVIRUS INFECTION			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
BACTERAEMIA			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	

CANDIDA INFECTION			
subjects affected / exposed	0 / 22 (0.00%)	3 / 69 (4.35%)	
occurrences (all)	0	3	
CELLULITIS			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
CLOSTRIDIUM DIFFICILE COLITIS			
subjects affected / exposed	1 / 22 (4.55%)	4 / 69 (5.80%)	
occurrences (all)	1	4	
CLOSTRIDIUM DIFFICILE INFECTION			
subjects affected / exposed	0 / 22 (0.00%)	3 / 69 (4.35%)	
occurrences (all)	0	3	
CYTOMEGALOVIRUS INFECTION			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
CYTOMEGALOVIRUS VIRAEMIA			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
ESCHERICHIA BACTERAEMIA			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
INCISION SITE CELLULITIS			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
INFECTION			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
MENINGITIS			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
MUCOSAL INFECTION			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
NASOPHARYNGITIS			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	

ORAL CANDIDIASIS				
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)		
occurrences (all)	0	1		
OROPHARYNGEAL CANDIDIASIS				
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)		
occurrences (all)	0	1		
PARONYCHIA				
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)		
occurrences (all)	0	1		
PNEUMONIA				
subjects affected / exposed	1 / 22 (4.55%)	7 / 69 (10.14%)		
occurrences (all)	1	7		
PNEUMONIA ADENOVIRAL				
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)		
occurrences (all)	0	1		
PNEUMONIA BACTERIAL				
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)		
occurrences (all)	0	1		
PNEUMONIA FUNGAL				
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)		
occurrences (all)	0	1		
RASH PUSTULAR				
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)		
occurrences (all)	0	1		
RESPIRATORY SYNCYTIAL VIRUS INFECTION				
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)		
occurrences (all)	0	1		
RHINITIS				
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)		
occurrences (all)	0	1		
RHINOVIRUS INFECTION				
subjects affected / exposed	0 / 22 (0.00%)	3 / 69 (4.35%)		
occurrences (all)	0	3		
SEPSIS				

subjects affected / exposed	1 / 22 (4.55%)	2 / 69 (2.90%)	
occurrences (all)	1	2	
SINUSITIS			
subjects affected / exposed	1 / 22 (4.55%)	2 / 69 (2.90%)	
occurrences (all)	1	2	
SKIN INFECTION			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
SOFT TISSUE INFECTION			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
STREPTOCOCCAL BACTERAEMIA			
subjects affected / exposed	0 / 22 (0.00%)	2 / 69 (2.90%)	
occurrences (all)	0	2	
STREPTOCOCCAL INFECTION			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
SUBCUTANEOUS ABSCESS			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	1 / 22 (4.55%)	5 / 69 (7.25%)	
occurrences (all)	1	5	
URINARY TRACT INFECTION			
subjects affected / exposed	1 / 22 (4.55%)	3 / 69 (4.35%)	
occurrences (all)	1	3	
Metabolism and nutrition disorders			
APPETITE DISORDER			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
DECREASED APPETITE			
subjects affected / exposed	6 / 22 (27.27%)	16 / 69 (23.19%)	
occurrences (all)	7	19	
DEHYDRATION			

subjects affected / exposed	2 / 22 (9.09%)	3 / 69 (4.35%)	
occurrences (all)	2	3	
ELECTROLYTE IMBALANCE			
subjects affected / exposed	0 / 22 (0.00%)	2 / 69 (2.90%)	
occurrences (all)	0	2	
FLUID OVERLOAD			
subjects affected / exposed	1 / 22 (4.55%)	4 / 69 (5.80%)	
occurrences (all)	1	4	
GOUT			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
HYPERAMMONAEMIA			
subjects affected / exposed	0 / 22 (0.00%)	2 / 69 (2.90%)	
occurrences (all)	0	2	
HYPERCALCAEMIA			
subjects affected / exposed	2 / 22 (9.09%)	2 / 69 (2.90%)	
occurrences (all)	4	4	
HYPERGLYCAEMIA			
subjects affected / exposed	8 / 22 (36.36%)	18 / 69 (26.09%)	
occurrences (all)	13	32	
HYPERKALAEMIA			
subjects affected / exposed	2 / 22 (9.09%)	7 / 69 (10.14%)	
occurrences (all)	3	8	
HYPERMAGNESAEMIA			
subjects affected / exposed	2 / 22 (9.09%)	3 / 69 (4.35%)	
occurrences (all)	3	5	
HYPERNATRAEMIA			
subjects affected / exposed	1 / 22 (4.55%)	2 / 69 (2.90%)	
occurrences (all)	1	4	
HYPERPHOSPHATAEMIA			
subjects affected / exposed	2 / 22 (9.09%)	5 / 69 (7.25%)	
occurrences (all)	2	5	
HYPERTRIGLYCERIDAEMIA			
subjects affected / exposed	4 / 22 (18.18%)	6 / 69 (8.70%)	
occurrences (all)	6	9	
HYPERURICAEMIA			

subjects affected / exposed	2 / 22 (9.09%)	2 / 69 (2.90%)	
occurrences (all)	3	3	
HYPOALBUMINAEMIA			
subjects affected / exposed	8 / 22 (36.36%)	16 / 69 (23.19%)	
occurrences (all)	13	26	
HYPOCALCAEMIA			
subjects affected / exposed	7 / 22 (31.82%)	19 / 69 (27.54%)	
occurrences (all)	9	32	
HYPOGLYCAEMIA			
subjects affected / exposed	3 / 22 (13.64%)	11 / 69 (15.94%)	
occurrences (all)	4	16	
HYPOKALAEMIA			
subjects affected / exposed	14 / 22 (63.64%)	37 / 69 (53.62%)	
occurrences (all)	17	59	
HYPOMAGNESAEMIA			
subjects affected / exposed	11 / 22 (50.00%)	21 / 69 (30.43%)	
occurrences (all)	14	29	
HYPONATRAEMIA			
subjects affected / exposed	8 / 22 (36.36%)	20 / 69 (28.99%)	
occurrences (all)	13	31	
HYPOPHOSPHATAEMIA			
subjects affected / exposed	9 / 22 (40.91%)	16 / 69 (23.19%)	
occurrences (all)	11	24	
HYPOVOLAEMIA			
subjects affected / exposed	0 / 22 (0.00%)	2 / 69 (2.90%)	
occurrences (all)	0	2	
INCREASED APPETITE			
subjects affected / exposed	0 / 22 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
INSULIN RESISTANCE			
subjects affected / exposed	1 / 22 (4.55%)	2 / 69 (2.90%)	
occurrences (all)	1	2	
TUMOUR LYSIS SYNDROME			
subjects affected / exposed	0 / 22 (0.00%)	2 / 69 (2.90%)	
occurrences (all)	0	2	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
12 March 2018	LL patient population added to the study, clarification that both relapsed and refractory populations of both ALL and LL were eligible for the study, updated the age range and added LL and ALL with Ph+ populations to the inclusion criteria, clarified exclusion criteria, updated meal and dietary requirements, added guidelines for outpatient monitoring of TLS, updates to list of excluded and cautionary medications.
29 March 2018	Updated TKI doses and differentiate pediatric doses from adult doses in Table 6, Added IM as alternative route of administration of pegasparaginase.
08 October 2018	Included secondary objective of number of subjects who proceed to CAR-T therapy, update to Study Design to change first day of chemotherapy administration to Day 1, updated exclusion criteria, updated requirements for lumbar puncture and radiographic scans, updated toxicity management.
23 October 2018	Updated protocol language to align with current venetoclax Standard Safety Risk Language.
12 March 2019	Added option of alternative steroids, added exception to Inclusion Criterion 3, updated throughout the protocol to indicate that subjects on venetoclax may enroll and remain on venetoclax, clarified toxicity management to indicate that venetoclax or navitoclax could be held at any time to allow for count recovery per investigator discretion.
29 August 2019	Pathology report added, allowed for lower doses of dexamethasone, updated and clarified inclusion and exclusion criteria, differentiated toxicity management guidelines for dose escalation subjects, clarified language regarding subjects who continued dosing beyond Week 37, reduced PK sample schedule for safety expansion cohort, added safety expansion cohort with intermittent dosing.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported