Clinical trial results:
A PHASE 3, MULTICENTER, OPEN-LABEL, RANDOMIZED STUDY COMPARING THE EFFICACY AND SAFETY OF AG-221 (CC-90007) VERSUS CONVENTIONAL CARE REGIMENS IN OLDER SUBJECTS WITH LATE STAGE ACUTE MYELOID LEUKEMIA HARBORING AN ISOCITRATE DEHYDROGENASE 2 MUTATION

Summary

EudraCT number	2015-000344-42
Trial protocol	DE GB ES DK BE AT CZ IT
Global end of trial date	25 March 2024

Results information

Result version number	v1 (current)
This version publication date	09 April 2025
First version publication date	09 April 2025

Trial information

Trial identification

Sponsor protocol code	AG-221-AML-004

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Bristol-Myers Squibb
Sponsor organisation address	Chaussée de la Hulpe 185, Brussels, Belgium, 1170
Public contact	Global Submission Management, Clinical Trials, Bristol-Myers Squibb International Corporation, mg-gsm-ct@bms.com
Scientific contact	Bristol-Myers Squibb Study Director, Bristol-Myers Squibb, mg-gsm-ct@bms.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?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	25 March 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	25 March 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study was to determine the primary efficacy, measured as OS, of enasidenib compared with CCRs in subjects 60 years or older with AML refractory to or relapsed after second- or third-line AML therapy and positive for an IDH2 mutation.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Conference on Harmonization Good Clinical Practice Guidelines. All the local regulatory requirements pertinent to safety of trial subjects were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	30 December 2015
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 9
Country: Number of subjects enrolled	Austria: 7
Country: Number of subjects enrolled	Belgium: 5
Country: Number of subjects enrolled	Brazil: 2
Country: Number of subjects enrolled	Canada: 15
Country: Number of subjects enrolled	China: 13
Country: Number of subjects enrolled	Czechia: 5
Country: Number of subjects enrolled	Denmark: 13
Country: Number of subjects enrolled	France: 54
Country: Number of subjects enrolled	Germany: 34
Country: Number of subjects enrolled	Italy: 20
Country: Number of subjects enrolled	Korea, Republic of: 6
Country: Number of subjects enrolled	Russian Federation: 15
Country: Number of subjects enrolled	Spain: 33
Country: Number of subjects enrolled	Taiwan: 5
Country: Number of subjects enrolled	Türkiye: 1
Country: Number of subjects enrolled	United Kingdom: 26
Country: Number of subjects enrolled	United States: 56

Worldwide total number of subjects	319
EEA total number of subjects	171

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)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	57
From 65 to 84 years	258
85 years and over	4

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

319 participants were randomized and 298 participants received treatment

Period 1

Period 1 title	Randomized Period
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	AG-221

Arm description:

Participants receive continuous 28-day cycles of AG-221 100 mg orally (PO) once a day (QD) for 28 days, plus best supportive care (BSC).

Arm type	Experimental
Investigational medicinal product name	AG-221
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

50mg, 100mg, 150mg, or 200mg

Arm title	Conventional Care Regimens (CCRs)

Arm description:

Treatment options include BSC only, azacitidine SC + BSC, LDAC SC + BSC, or IDAC IV + BSC. BSC only: 28-day cycles including hydroxyurea (for leukocytosis/IDH syndrome), anti-infectives, analgesics, antiemetics, and nutritional support. AZA+BSC: Azacitidine 775 mg/m2/day SC for 7 days plus BSC in 28-day cycles. LDAC+BSC: Cytarabine 20 mg SC BID for 10 days plus BSC in 28-day cycles. IDAC+BSC: Cytarabine 0.5–1.5 g/m2/day IV for 3–6 days per institutional practice, followed by BSC. The content guides on treatments for hematologic disorders with varied dosing, combining supportive care to improve patient outcomes while considering institutional protocols.

Arm type	Experimental
Investigational medicinal product name	Low-Dose Cytarabine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravascular use

Dosage and administration details:

Subjects randomized to the LDAC treatment option will receive continuous 28-day cycles of cytarabine 20 mg SC BID for 10 days until the End of Trial.

Subjects randomized to IDAC treatment option will receive 28-day cycles of cytarabine 0.5 to 1.5 g/m2/day IV for 3 to 6 days, per standard institutional practice, unless they are discontinued from the study treatment.

Investigational medicinal product name	Azacitidine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for suspension for injection

Routes of administration	Subcutaneous use

Dosage and administration details:

100mg

Number of subjects in period 1	AG-221	Conventional Care Regimens (CCRs)
Started	158	161
Completed	157	141
Not completed	1	20
Adverse event, serious fatal	1	-
Other reasons	-	20

Period 2

Period 2 title	Treatment Period
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	AG-221

Arm description:

Participants receive continuous 28-day cycles of AG-221 100 mg orally (PO) once a day (QD) for 28 days, plus best supportive care (BSC).

Arm type	Experimental
Investigational medicinal product name	AG-221
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

50mg, 100mg, 150mg, or 200mg

Arm title	Conventional Care Regimens (CCRs)

Arm description:

Treatment options include BSC only, azacitidine SC + BSC, LDAC SC + BSC, or IDAC IV + BSC. BSC only: 28-day cycles including hydroxyurea (for leukocytosis/IDH syndrome), anti-infectives, analgesics, antiemetics, and nutritional support. AZA+BSC: Azacitidine 775 mg/m2/day SC for 7 days plus BSC in 28-day cycles. LDAC+BSC: Cytarabine 20 mg SC BID for 10 days plus BSC in 28-day cycles. IDAC+BSC: Cytarabine 0.5–1.5 g/m2/day IV for 3–6 days per institutional practice, followed by BSC. The content guides on treatments for hematologic disorders with varied dosing, combining supportive care to improve patient outcomes while considering institutional protocols.

Arm type	Active comparator

Investigational medicinal product name	Low-Dose Cytarabine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravascular use

Dosage and administration details:

Subjects randomized to the LDAC treatment option will receive continuous 28-day cycles of cytarabine 20 mg SC BID for 10 days until the End of Trial. Subjects randomized to IDAC treatment option will receive 28-day cycles of cytarabine 0.5 to 1.5 g/m2/day IV for 3 to 6 days, per standard institutional practice, unless they are discontinued from the study treatment.

Investigational medicinal product name	Azacitidine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for suspension for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

100mg

Number of subjects in period 2	AG-221	Conventional Care Regimens (CCRs)
Started	157	141
Completed	0	0
Not completed	157	141
Adverse event, serious fatal	38	23
Transition to commercially available treatment	1	1
Consent withdrawn by subject	10	24
Physician decision	1	-
Disease Relapse	28	1
Adverse event, non-fatal	17	12
Progressive Disease	53	37
Other reasons	3	39
Hematopoietic Stem Cell Transplantation	6	2
Lost to follow-up	-	1
Protocol deviation	-	1

Baseline characteristics

Reporting groups	
Reporting group title	AG-221
Reporting group description:	
Participants receive continuous 28-day cycles of AG-221 100 mg orally (PO) once a day (QD) for 28 days, plus best supportive care (BSC).	
Reporting group title	Conventional Care Regimens (CCRs)
Reporting group description:	
Treatment options include BSC only, azacitidine SC + BSC, LDAC SC + BSC, or IDAC IV + BSC. BSC only: 28-day cycles including hydroxyurea (for leukocytosis/IDH syndrome), anti-infectives, analgesics, antiemetics, and nutritional support. AZA+BSC: Azacitidine 775 mg/m2/day SC for 7 days plus BSC in 28-day cycles. LDAC+BSC: Cytarabine 20 mg SC BID for 10 days plus BSC in 28-day cycles. IDAC+BSC: Cytarabine 0.5–1.5 g/m2/day IV for 3–6 days per institutional practice, followed by BSC. The content guides on treatments for hematologic disorders with varied dosing, combining supportive care to improve patient outcomes while considering institutional protocols.	

Reporting group values	AG-221	Conventional Care Regimens (CCRs)	Total
Number of subjects	158	161	319
Age Categorical Units: Participants			
≥ 60 to < 70 years	61	72	133
≥ 70 to < 80 years	80	77	157
≥ 80 years	17	12	29
Age Continuous Units: Years			
arithmetic mean	71.4	70.5	
standard deviation	± 6.04	± 6.17	-
Sex: Female, Male Units: Participants			
Female	67	65	132
Male	91	96	187
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	12	12	24
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	2	6	8
White	115	110	225
More than one race	0	0	0
Unknown or Not Reported	29	33	62
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	4	3	7
Not Hispanic or Latino	126	128	254
Unknown or Not Reported	28	30	58

End points

End points reporting groups

Reporting group title	AG-221
Reporting group description:	
Participants receive continuous 28-day cycles of AG-221 100 mg orally (PO) once a day (QD) for 28 days, plus best supportive care (BSC).	
Reporting group title	Conventional Care Regimens (CCRs)
Reporting group description:	
Treatment options include BSC only, azacitidine SC + BSC, LDAC SC + BSC, or IDAC IV + BSC. BSC only: 28-day cycles including hydroxyurea (for leukocytosis/IDH syndrome), anti-infectives, analgesics, antiemetics, and nutritional support. AZA+BSC: Azacitidine 775 mg/m2/day SC for 7 days plus BSC in 28-day cycles. LDAC+BSC: Cytarabine 20 mg SC BID for 10 days plus BSC in 28-day cycles. IDAC+BSC: Cytarabine 0.5–1.5 g/m2/day IV for 3–6 days per institutional practice, followed by BSC. The content guides on treatments for hematologic disorders with varied dosing, combining supportive care to improve patient outcomes while considering institutional protocols.	
Reporting group title	AG-221
Reporting group description:	
Participants receive continuous 28-day cycles of AG-221 100 mg orally (PO) once a day (QD) for 28 days, plus best supportive care (BSC).	
Reporting group title	Conventional Care Regimens (CCRs)
Reporting group description:	
Treatment options include BSC only, azacitidine SC + BSC, LDAC SC + BSC, or IDAC IV + BSC. BSC only: 28-day cycles including hydroxyurea (for leukocytosis/IDH syndrome), anti-infectives, analgesics, antiemetics, and nutritional support. AZA+BSC: Azacitidine 775 mg/m2/day SC for 7 days plus BSC in 28-day cycles. LDAC+BSC: Cytarabine 20 mg SC BID for 10 days plus BSC in 28-day cycles. IDAC+BSC: Cytarabine 0.5–1.5 g/m2/day IV for 3–6 days per institutional practice, followed by BSC. The content guides on treatments for hematologic disorders with varied dosing, combining supportive care to improve patient outcomes while considering institutional protocols.	

Primary: Overall Survival (OS)

End point title	Overall Survival (OS)
End point description:	
The time between randomization and death from any cause. Participants who drop-out or are alive at the end of trial will have their OS times censored at the time of last contact, as appropriate.	
End point type	Primary
End point timeframe:	
From randomization to death due to any cause (up to approximately 49 months)	

End point values	AG-221	Conventional Care Regimens (CCRs)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	158	161		
Units: Months				
median (confidence interval 95%)	6.5 (5.5 to 9.5)	6.2 (4.6 to 7.7)		

Statistical analyses

Statistical analysis title	Statistical Analysis for Primary OS
Comparison groups	Conventional Care Regimens (CCRs) v AG-221
Number of subjects included in analysis	319
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.2288
Method	Stratified Log Rank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.86
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.67
upper limit	1.1

Secondary: Overall Response Rate

End point title	Overall Response Rate

End point description:

Number of participants with MLFS + CR + CRi + CRp + PR according to modified International Working Group Acute Myeloid Leukemia (IWG AML) response criteria. Complete response (CR) and morphologic leukemia-free state (MLFS) are defined as <5% blasts in a BM aspirate sample with marrow spicules and a count of ≥200 nucleated cells. There should be no blasts with Auer rods and no extramedullary disease. CR must also include: absolute neutrophil count (ANC) ≥1,000/µL, Platelet count ≥100,000/µL, and independent of red cell transfusions for ≥1 week before each response assessment. Complete remission with incomplete neutrophil recovery (CRi) is all criteria of CR except ANC. Complete remission with incomplete platelet recovery (CRp) is all criteria of CR except platelet count. Partial remission (PR) is defined as all hematologic criteria of CR with a >50% decrease in the percentage of BM blasts to 5% to 25%. (<5% considered if Auer rods are present).

End point type	Secondary

End point timeframe:

From randomization up to approximately 99 months

End point values	AG-221	Conventional Care Regimens (CCRs)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	158	161		
Units: Count of Subjects	64	16		

Statistical analyses

Statistical analysis title	Statistical Analysis for ORR
Comparison groups	AG-221 v Conventional Care Regimens (CCRs)

Number of subjects included in analysis	319
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001 [1]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	6.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.32
upper limit	11.14

Notes:

[1] - p-value from a Cochran-Mantel-Haenszel test comparing the response rates between the AG-221 group and the combined CCR group with stratification factors of prior intensive therapy for AML and primary refractory status

Secondary: Event-Free Survival

End point title	Event-Free Survival

End point description:

Time from randomization to documented morphologic relapse after complete remission/complete remission with incomplete neutrophil recovery/complete remission with incomplete platelet recovery (CR/CRi/CRp), progressive disease (PD) or death from any cause, whichever occurs first. Morphologic Relapse after CR/CRi/CRp is defined as either reappearance of ≥ 5% blasts in the BM not attributable to any other cause or the development of extramedullary disease. PD is defined as a > 50% increase of BM blast count percentage from baseline to ≥ 20% for participants with 5 to 70% BM blasts at baseline or a doubling of absolute blast count in peripheral blood from baseline to ≥ 10 x 109/L (10,000/µL) for participants with > 70% BM blasts at baseline or the development of new extramedullary disease.

End point type	Secondary

End point timeframe:

From randomization to the date of documented morphologic relapse after CR/CRi/CRp, PD or death from any cause, whichever occurs first. (up to approximately 49 months)

End point values	AG-221	Conventional Care Regimens (CCRs)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	158	161		
Units: Months				
median (confidence interval 95%)	4.9 (3.7 to 5.9)	2.6 (1.9 to 4.4)		

Statistical analyses

Statistical analysis title	Statistical Analysis for EFS
Comparison groups	AG-221 v Conventional Care Regimens (CCRs)

Number of subjects included in analysis	319
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.02
Method	Stratified Log Rank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.73
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.55
upper limit	0.95

Secondary: Treatment Mortality at 30 Days

End point title	Treatment Mortality at 30 Days

End point description:

The number of participant deaths from any cause within 30 days of initiation of study treatment.

End point type	Secondary

End point timeframe:

From first dose to 30 days after first dose

End point values	AG-221	Conventional Care Regimens (CCRs)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	158	161		
Units: Participants	10	13		

Statistical analyses

No statistical analyses for this end point

Secondary: Treatment Mortality at 60 Days

End point title	Treatment Mortality at 60 Days

End point description:

The number of participant deaths from any cause within 60 days of initiation of study treatment.

End point type	Secondary

End point timeframe:

From first dose to 60 days after first dose

End point values	AG-221	Conventional Care Regimens (CCRs)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	158	161		
Units: Participants	27	30		

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response

End point title	Duration of Response

End point description:

Time from first documented response (MLFS/CR/CRi/CRp/PR) to morphologic relapse, progression, or death, whichever occurs first. CR/MLFS: <5% BM blasts in spicules with ≥200 nucleated cells, no Auer rod blasts, no extramedullary disease. CR also requires ANC ≥1,000/µL, platelets ≥100,000/µL, and no transfusions for ≥1 week. CRi excludes ANC; CRp excludes platelets. PR: All CR hematologic criteria with >50% BM blast decrease to 5-25%. Relapse (CR/CRi/CRp): BM blasts reappear ≥5% or extramedullary disease develops. PD: >50% BM blast increase to ≥20%, blood blasts double to ≥10,000/µL, or new extramedullary disease.
Here "99999" means NA

End point type	Secondary

End point timeframe:

From randomization to documented morphologic relapse after CR/CRi/CRp/ PD or death due to any cause, whichever occurs first (up to approximately 49 months)

End point values	AG-221	Conventional Care Regimens (CCRs)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	64	16		
Units: Months				
median (confidence interval 95%)	7.4 (5.6 to 12.7)	33.3 (2.5 to 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Response

End point title	Time to Response

End point description:

Time from randomization to first documented MLFS/CR/CRi/CRp/PR. Complete remission (CR) and morphologic leukemia-free state (MLFS) are defined as <5% blasts in a BM aspirate sample with marrow spicules and a count of ≥200 nucleated cells. There should be no blasts with Auer rods and no extramedullary disease. CR must also include the following conditions: absolute neutrophil count (ANC) ≥1,000/µL, Platelet count ≥100,000/µL, and independent of red cell transfusions for ≥1 week before each response assessment. Complete remission with incomplete neutrophil recovery (CRi) is all criteria

of CR except ANC. Complete remission with incomplete platelet recovery (CRp) is all criteria of CR except platelet count. partial remission (PR) is defined as all hematologic criteria of CR with a >50% decrease in the percentage of BM blasts to 5% to 25%. (<5% considered if Auer rods are present).

End point type	Secondary

End point timeframe:

From randomization to to first documented MLFS/CR/CRi/CRp/PR (up to approximately 49 months)

End point values	AG-221	Conventional Care Regimens (CCRs)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25	7		
Units: Days				
median (full range (min-max))	58.0 (23 to 242)	56.0 (27 to 63)		

Statistical analyses

No statistical analyses for this end point

Secondary: One-Year Survival Rate

End point title	One-Year Survival Rate

End point description:

The proportion of participants alive at 1 year after randomization

End point type	Secondary

End point timeframe:

From randomization to 1 year after randomization

End point values	AG-221	Conventional Care Regimens (CCRs)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	158	161		
Units: Proportion of participants				
number (confidence interval 95%)	0.379 (0.303 to 0.454)	0.263 (0.193 to 0.337)		

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Remission Rate

End point title	Overall Remission Rate

End point description:

The number of participants with CR + CRi + CRp according to modified International Working Group Acute Myeloid Leukemia (IWG AML) response criteria. Complete remission (CR) is defined as <5% blasts in a BM aspirate sample with marrow spicules and a count of ≥200 nucleated cells. There should be no blasts with Auer rods and no extramedullary disease. CR must also include the following conditions: absolute neutrophil count (ANC) ≥1,000/µL, Platelet count ≥100,000/µL, and independent of red cell transfusions for ≥1 week before each response assessment. Complete remission with incomplete neutrophil recovery (CRi) is all criteria of CR except ANC. Complete remission with incomplete platelet recovery (CRp) is all criteria of CR except platelet count.

End point type	Secondary

End point timeframe:

From randomization up to approximately 49 months

End point values	AG-221	Conventional Care Regimens (CCRs)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	158	161		
Units: Participants	47	10		

Statistical analyses

Statistical analysis title	Statistical Analysis for Overall Remission Rate
Comparison groups	AG-221 v Conventional Care Regimens (CCRs)
Number of subjects included in analysis	319
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Fisher exact

Secondary: Hematologic Improvement Rate

End point title	Hematologic Improvement Rate

End point description:

The number of participants with hematologic improvement neutrophil response (HI-N) + hematologic improvement platelet response (HI-P) + hematologic improvement erythroid response (HI-E) according to the International Working Group for Myelodysplastic Syndromes for Hematologic Improvement (IWG MDS HI) criteria. HI-E is defined as a hemoglobin increase by ≥ 1.5 g/dL and a relevant reduction in units of RBC transfusions by an absolute number of at least 4 RBC transfusions/8 week compared with the pretreatment transfusion number in the previous 8 week. HI-P is defined as an absolute increase of ≥ 30 X 10^9/L for participants starting with > 20 X and an increase from < 20 X 10^9/L to > 20 X 10^9/L and by at least 100%. HI-N is defined as At least 100% increase and an absolute increase > 0.5 X 10^9/L.

End point type	Secondary

End point timeframe:

From randomization up to approximately 49 months

End point values	AG-221	Conventional Care Regimens (CCRs)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	158	161		
Units: Participants	67	18		

Statistical analyses

Statistical analysis title	Statistical Analysis for HIR
Comparison groups	AG-221 v Conventional Care Regimens (CCRs)
Number of subjects included in analysis	319
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Fisher exact

Secondary: The Number of Participants that Underwent Hematopoietic Stem Cell Transplantation (HSCT)

End point title	The Number of Participants that Underwent Hematopoietic Stem Cell Transplantation (HSCT)

End point description:

The number of participants that underwent hematopoietic stem cell transplantation during the study.

End point type	Secondary

End point timeframe:

From randomization up to approximately 49 months

End point values	AG-221	Conventional Care Regimens (CCRs)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	158	161		
Units: Participants	7	2		

Statistical analyses

No statistical analyses for this end point

Secondary: Complete Remission Rate

End point title	Complete Remission Rate

End point description:

The number of participants with morphologic complete remission (CR) according to modified International Working Group Acute Myeloid Leukemia Response Criteria (IWG AML). CR is defined as less than 5% blasts in a BM aspirate sample with marrow spicules and with a count of at least 200

nucleated cells. There should be no blasts with Auer rods and absence of extramedullary disease; plus the following conditions: absolute neutrophil count (ANC) ≥1,000/µL, Platelet count ≥100,000/µL, and independent of red cell transfusions for ≥1 week before each response assessment.

End point type	Secondary

End point timeframe:

From randomization up to approximately 49 months

End point values	AG-221	Conventional Care Regimens (CCRs)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	158	161		
Units: Participants	37	6		

Statistical analyses

Statistical analysis title	Statistical Analysis for CRR
Comparison groups	AG-221 v Conventional Care Regimens (CCRs)
Number of subjects included in analysis	319
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Fisher exact

Secondary: Time to Treatment Failure

End point title	Time to Treatment Failure

End point description:

Time from randomization to discontinuation of study treatment due to any cause

End point type	Secondary

End point timeframe:

From randomization to discontinuation of study treatment due to any cause (up to approximately 49 months)

End point values	AG-221	Conventional Care Regimens (CCRs)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	158	161		
Units: Months				
median (confidence interval 95%)	4.9 (4.0 to 6.0)	1.9 (1.4 to 2.5)		

Statistical analyses

Statistical analysis title	Statistical Analysis for Time to Treatment Failure
Comparison groups	AG-221 v Conventional Care Regimens (CCRs)
Number of subjects included in analysis	319
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Stratified Log Rank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.53
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.41
upper limit	0.67

Secondary: The Number of Participants Experiencing Adverse Events (AEs)

End point title	The Number of Participants Experiencing Adverse Events (AEs)

End point description:

The number of participants experiencing different types of adverse events (AE). An AE is any noxious, unintended, or untoward medical occurrence that may appear or worsen in a participant during the course of a study. A Serious Adverse Event (SAE) is any AE occurring at any dose that: results in death, is life-threatening, requires inpatient hospitalization or prolongation of existing hospitalization, results in persistent or significant disability/incapacity, is a congenital anomaly/birth defect, or constitutes an important medical event. All AEs were coded using the MedDRA Version 22.0. Adverse events were analyzed in terms of treatment-emergent AEs (TEAEs). A treatment-related TEAE was defined as a TEAE that was suspected by the investigator to be related to study treatment. The severity was graded by the study personnel based on NCI National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE) Version 4.03.

TR= Treatment Related
DI= Dose Interruption

End point type	Secondary

End point timeframe:

Please fill in

End point values	AG-221	Conventional Care Regimens (CCRs)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	157	141		
Units: Participants				
Treatment-Emergent Adverse Event (TEAE)	157	131		
TEAE Related to Study Drug	122	86		
Grade ≥ 3 TEAE	148	112		
Grade ≥ 3 TEAE Related to Study Drug	75	49		
Serious TEAE	139	92		
Serious TEAE Related to Study Drug	34	30		
TEAE Leading to Discontinuation of Study Drug	38	16		
TR TEAE Leading to Discontinuation of Study Drug	5	6		
TEAE Leading to Study Drug Dose Reduction Only	22	3		
TR TEAE Leading to Study Drug Dose Reduction Only	18	3		
TEAE Leading to Study Drug Dose Interruption Only	85	36		
TR TEAE Leading to Study Drug DI Only	46	21		
TEAE Leading to Study Drug Dose Reduction or DI	92	37		
TR TEAE Leading to Study Drug Dose Reduction or DI	56	22		
TEAE Leading to Death	79	33		
Treatment-related TEAE Leading to Death	1	5		

Statistical analyses

No statistical analyses for this end point

Secondary: The Percent of Participants Experiencing Clinically Significant Laboratory Abnormalities - Serum Chemistry

End point title	The Percent of Participants Experiencing Clinically Significant Laboratory Abnormalities - Serum Chemistry

End point description:

The percent of participants with clinically significant serum chemistry laboratory abnormalities. A clinically significant laboratory abnormality is defined as meeting Grade 3 or Grade 4 criteria according to the Common Terminology Criteria for Adverse Events (CTCAE). Grade 3 is defined as severe or medically significant but not immediately life threatening; hospitalization or prolongation of hospitalization indicated; disabling; limiting self care. Grade 4 is defined as life-threatening consequences; urgent intervention indicated. The chemistry panel includes sodium, potassium, calcium, magnesium, chloride, phosphorus, CO2, bicarbonate, blood urea nitrogen (BUN), creatinine, glucose, albumin, total protein, alkaline phosphatase (ALP), bilirubin (total and direct), uric acid, lactate dehydrogenase (LDH), AST/SGOT, ALT/SGPT, gamma glutamyl transpeptidase (GGT), amylase and lipase.

End point type	Secondary

End point timeframe:

From first dose up to approximately 49 months

End point values	AG-221	Conventional Care Regimens (CCRs)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	157	141		
Units: Percent of Participants				
number (not applicable)	42.7	21.3		

Statistical analyses

No statistical analyses for this end point

Secondary: The Percent of Participants Experiencing Clinically Significant Laboratory Abnormalities - Hematology

End point title	The Percent of Participants Experiencing Clinically Significant Laboratory Abnormalities - Hematology

End point description:

The percent of participants with clinically significant hematology laboratory abnormalities. A clinically significant laboratory abnormality is defined as meeting Grade 3 or Grade 4 criteria according to the Common Terminology Criteria for Adverse Events (CTCAE). Grade 3 is defined as severe or medically significant but not immediately life threatening; hospitalization or prolongation of hospitalization indicated; disabling; limiting self care. Grade 4 is defined as life-threatening consequences; urgent intervention indicated. The hematology panel includes complete blood count (CBC) with differential, including red blood cell (RBC) count, hemoglobin, hematocrit, mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), white blood cell (WBC) count (with differential), absolute neutrophil count (ANC) and platelet count.

End point type	Secondary

End point timeframe:

From first dose up to approximately 49 months

End point values	AG-221	Conventional Care Regimens (CCRs)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	157	141		
Units: Percent of Participants				
number (not applicable)	94.3	89.4		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in the European Organization for Research and Treatment of Cancer Quality-of-Life questionnaire (EORTC QLQ-C30)

End point title	Change from Baseline in the European Organization for Research and Treatment of Cancer Quality-of-Life questionnaire (EORTC QLQ-C30)

End point description:

The change from baseline in the EORTC QLQ-C30 questionnaire. The EORTC QLQ-C30 is composed of 30 items that address general physical symptoms, physical functioning, fatigue and malaise, and social and emotional functioning. Subscale scores are transformed to a 0 to 100 scale, with higher scores on functional scales indicating better function and higher scores on symptom scales indicating worse symptoms. A change of at least 10 points on the standardized domain scores was required for it to be considered meaningful. Results obtained just prior to the start of study treatment on Day 1 of Cycle 1 will serve as the baseline values. If not available, the most recent screening results prior to the start of study treatment on Day 1 of Cycle 1 will be considered the baseline values.

End point type	Secondary

End point timeframe:

From baseline to cycle 2 day 1 (up to approximately 1 month)

End point values	AG-221	Conventional Care Regimens (CCRs)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	106	62		
Units: Change from baseline in QLQ-C30 score				
arithmetic mean (standard deviation)				
Global QoL	-4.7 (± 20.18)	-4.0 (± 18.46)		
Physical Functioning	-3.1 (± 17.19)	-6.7 (± 21.32)		
Role Functioning	-3.8 (± 27.63)	-7.8 (± 29.98)		
Cognitive Functioning	-0.6 (± 16.89)	-5.1 (± 18.00)		
Emotional Functioning	0.9 (± 15.72)	-0.7 (± 18.44)		
Social Functioning	-0.6 (± 29.27)	-10.2 (± 31.56)		
Fatigue	5.5 (± 18.73)	7.5 (± 25.59)		
Nausea / Vomiting	9.0 (± 20.21)	1.9 (± 15.12)		
Pain	6.0 (± 23.37)	7.0 (± 30.11)		
Dyspnea	-1.3 (± 23.42)	0.0 (± 27.66)		
Insomnia	8.5 (± 26.85)	1.1 (± 33.04)		
Appetite Loss	10.7 (± 28.19)	8.6 (± 31.33)		
Constipation	2.8 (± 24.82)	1.6 (± 24.46)		
Diarrhea	4.1 (± 24.21)	1.6 (± 18.53)		
Financial Difficulties	-0.3 (± 24.12)	-3.2 (± 21.52)		

Statistical analyses

No statistical analyses for this end point

Secondary: The Percentage of Participants Experiencing Clinically Significant Electrocardiogram (ECG) Abnormalities

End point title	The Percentage of Participants Experiencing Clinically Significant Electrocardiogram (ECG) Abnormalities

End point description:

The percent of participants with clinically significant ECG abnormalities. 12-lead ECG was assessed by a

physician trained in ECG interpretation. Intervals including PR, QRS, QT and RR were collected, as well as heart rate and rhythm.

End point type	Secondary

End point timeframe:

From first dose up to approximately 49 months

End point values	AG-221	Conventional Care Regimens (CCRs)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	147	120		
Units: Percentage of Participants				
number (not applicable)	7.6	2.1		

Statistical analyses

No statistical analyses for this end point

Secondary: The Percent of Participants Experiencing Clinically Significant Vital Sign Abnormalities

End point title	The Percent of Participants Experiencing Clinically Significant Vital Sign Abnormalities

End point description:

The percent of participants with clinically significant vital sign abnormalities including weight, temperature, blood pressure, pulse rate, and respiratory rate.

End point type	Secondary

End point timeframe:

From first dose up to approximately 49 months

End point values	AG-221	Conventional Care Regimens (CCRs)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	157	141		
Units: Percent of Participants	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in EQ-5D-5L Health Utility Index

End point title	Change from Baseline in EQ-5D-5L Health Utility Index

End point description:

The European Quality of Life 5D-5L Scale (EQ-5D-5L) assesses general health-related quality of life. Health is defined in 5 dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Each dimension has 5 levels: no problems, slight problems, moderate problems, severe problems, and extreme problems. Responses are coded so that a '1' indicates no problem, and '5' indicates the most serious problem. The responses for the 5 dimensions are combined in a 5-digit number. These health states are converted to a single index value using the crosswalk method to the EQ-5D-3L value set from the United Kingdom (UK). The EQ-5D-3L health utility index based on the UK population weights range from -0.594 to 1.0 with higher scores indicating higher health utility. Baseline results are obtained just prior to the start of study treatment on Day 1 of Cycle 1 and will serve as the baseline values.

End point type	Secondary

End point timeframe:

From baseline up to cycle 2 day 1 (up to approximately 1 month)

End point values	AG-221	Conventional Care Regimens (CCRs)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	106	62		
Units: Change from baseline in EQ-5D score				
arithmetic mean (standard deviation)	-0.0738 (± 0.2128)	-0.0598 (± 0.2500)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Serious Adverse Events and Other (Not Including Serious) Adverse Events were collected form from first dose to 28 days after last dose (up to approximately 49 months).

Adverse event reporting additional description:

Serious Adverse Events and Other (Not Including Serious) Adverse Events were assessed/monitored for the treated population. All-Cause Mortality was assessed for the randomized population.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	26.1

Reporting groups

Reporting group title	AG-221

Reporting group description:

Participants receive continuous 28-day cycles of AG-221 100 mg orally (PO) once a day (QD) for 28 days, plus best supportive care (BSC).

Reporting group title	BSC Only

Reporting group description:

continuous 28-day cycles of BSC

Reporting group title	Azacitidine + BSC

Reporting group description:

continuous 28-day cycles of azacitidine 75 mg/m2/day SC for 7 days, plus BSC

Reporting group title	LDAC + BSC

Reporting group description:

continuous 28-day cycles of cytarabine 20 mg SC BID for 10 days, plus BSC

Reporting group title	IDAC + BSC

Reporting group description:

28-day cycles of cytarabine 0.5 to 1.5 g/m2/day IV for 3 to 6 days, per standard institutional practice, plus BSC; only BSC given after IDAC therapy concludes per standard institutional practice.

Serious adverse events	AG-221	BSC Only	Azacitidine + BSC
Total subjects affected by serious adverse events			
subjects affected / exposed	139 / 157 (88.54%)	10 / 22 (45.45%)	38 / 58 (65.52%)
number of deaths (all causes)	143	20	53
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
ACUTE LEUKAEMIA			
subjects affected / exposed	1 / 157 (0.64%)	0 / 22 (0.00%)	0 / 58 (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
GASTRIC CANCER			

subjects affected / exposed	1 / 157 (0.64%)	0 / 22 (0.00%)	0 / 58 (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
ONCOLOGIC COMPLICATION			
subjects affected / exposed	2 / 157 (1.27%)	0 / 22 (0.00%)	1 / 58 (1.72%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 2	0 / 0	0 / 1
SQUAMOUS CELL CARCINOMA			
subjects affected / exposed	0 / 157 (0.00%)	0 / 22 (0.00%)	1 / 58 (1.72%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SQUAMOUS CELL CARCINOMA OF SKIN			
subjects affected / exposed	1 / 157 (0.64%)	0 / 22 (0.00%)	0 / 58 (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
ACUTE LYMPHOCYTIC LEUKAEMIA			
subjects affected / exposed	1 / 157 (0.64%)	0 / 22 (0.00%)	0 / 58 (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
ACUTE MYELOID LEUKAEMIA			
subjects affected / exposed	6 / 157 (3.82%)	0 / 22 (0.00%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	0 / 6	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 5	0 / 0	0 / 0
ACUTE MYELOID LEUKAEMIA RECURRENT			
subjects affected / exposed	1 / 157 (0.64%)	0 / 22 (0.00%)	0 / 58 (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
DIFFERENTIATION SYNDROME			
subjects affected / exposed	9 / 157 (5.73%)	0 / 22 (0.00%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	9 / 9	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ENDOMETRIAL CANCER			

subjects affected / exposed	1 / 157 (0.64%)	0 / 22 (0.00%)	0 / 58 (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 disorders			
HAEMORRHAGE			
subjects affected / exposed	1 / 157 (0.64%)	0 / 22 (0.00%)	0 / 58 (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
HYPOTENSION			
subjects affected / exposed	6 / 157 (3.82%)	0 / 22 (0.00%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	0 / 6	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
ASTHENIA			
subjects affected / exposed	2 / 157 (1.27%)	0 / 22 (0.00%)	0 / 58 (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
FATIGUE			
subjects affected / exposed	4 / 157 (2.55%)	0 / 22 (0.00%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	0 / 5	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GENERAL PHYSICAL HEALTH DETERIORATION			
subjects affected / exposed	14 / 157 (8.92%)	1 / 22 (4.55%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	0 / 15	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 8	0 / 0	0 / 0
PYREXIA			
subjects affected / exposed	15 / 157 (9.55%)	0 / 22 (0.00%)	2 / 58 (3.45%)
occurrences causally related to treatment / all	1 / 18	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
INFLUENZA LIKE ILLNESS			
subjects affected / exposed	0 / 157 (0.00%)	0 / 22 (0.00%)	1 / 58 (1.72%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

MALAISE			
subjects affected / exposed	1 / 157 (0.64%)	0 / 22 (0.00%)	0 / 58 (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
MUCOSAL INFLAMMATION			
subjects affected / exposed	1 / 157 (0.64%)	0 / 22 (0.00%)	0 / 58 (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
MULTIPLE ORGAN DYSFUNCTION SYNDROME			
subjects affected / exposed	3 / 157 (1.91%)	1 / 22 (4.55%)	1 / 58 (1.72%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 3	0 / 0	0 / 1
ORGAN FAILURE			
subjects affected / exposed	0 / 157 (0.00%)	0 / 22 (0.00%)	1 / 58 (1.72%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
PHYSICAL DECONDITIONING			
subjects affected / exposed	1 / 157 (0.64%)	0 / 22 (0.00%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
GRAFT VERSUS HOST DISEASE			
subjects affected / exposed	0 / 157 (0.00%)	0 / 22 (0.00%)	1 / 58 (1.72%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
BENIGN PROSTATIC HYPERPLASIA			
subjects affected / exposed	0 / 157 (0.00%)	0 / 22 (0.00%)	1 / 58 (1.72%)
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	0 / 157 (0.00%)	0 / 22 (0.00%)	1 / 58 (1.72%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CHRONIC OBSTRUCTIVE PULMONARY DISEASE			
subjects affected / exposed	1 / 157 (0.64%)	0 / 22 (0.00%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LUNG INFILTRATION			
subjects affected / exposed	1 / 157 (0.64%)	0 / 22 (0.00%)	0 / 58 (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
LUNG DISORDER			
subjects affected / exposed	2 / 157 (1.27%)	1 / 22 (4.55%)	1 / 58 (1.72%)
occurrences causally related to treatment / all	0 / 2	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
EPISTAXIS			
subjects affected / exposed	3 / 157 (1.91%)	0 / 22 (0.00%)	1 / 58 (1.72%)
occurrences causally related to treatment / all	1 / 3	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DYSPNOEA			
subjects affected / exposed	2 / 157 (1.27%)	0 / 22 (0.00%)	1 / 58 (1.72%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ORGANISING PNEUMONIA			
subjects affected / exposed	1 / 157 (0.64%)	0 / 22 (0.00%)	0 / 58 (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
PLEURAL EFFUSION			
subjects affected / exposed	1 / 157 (0.64%)	0 / 22 (0.00%)	2 / 58 (3.45%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
PNEUMONITIS			

subjects affected / exposed	1 / 157 (0.64%)	0 / 22 (0.00%)	0 / 58 (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	3 / 157 (1.91%)	0 / 22 (0.00%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 2	0 / 0	0 / 0
RESPIRATORY FAILURE			
subjects affected / exposed	4 / 157 (2.55%)	0 / 22 (0.00%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	1 / 5	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 2	0 / 0	0 / 0
Psychiatric disorders			
CONFUSIONAL STATE			
subjects affected / exposed	1 / 157 (0.64%)	0 / 22 (0.00%)	0 / 58 (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
Investigations			
BLAST CELL COUNT INCREASED			
subjects affected / exposed	1 / 157 (0.64%)	0 / 22 (0.00%)	2 / 58 (3.45%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
ALANINE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	1 / 157 (0.64%)	0 / 22 (0.00%)	0 / 58 (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
LIVER FUNCTION TEST INCREASED			
subjects affected / exposed	1 / 157 (0.64%)	0 / 22 (0.00%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BLOOD CREATININE INCREASED			
subjects affected / exposed	1 / 157 (0.64%)	0 / 22 (0.00%)	0 / 58 (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

EJECTION FRACTION DECREASED			
subjects affected / exposed	1 / 157 (0.64%)	0 / 22 (0.00%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GENERAL PHYSICAL CONDITION ABNORMAL			
subjects affected / exposed	1 / 157 (0.64%)	0 / 22 (0.00%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BLOOD BILIRUBIN INCREASED			
subjects affected / exposed	1 / 157 (0.64%)	0 / 22 (0.00%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
TRANSAMINASES INCREASED			
subjects affected / exposed	1 / 157 (0.64%)	0 / 22 (0.00%)	0 / 58 (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
PLATELET COUNT DECREASED			
subjects affected / exposed	1 / 157 (0.64%)	0 / 22 (0.00%)	0 / 58 (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
Injury, poisoning and procedural complications			
ANAPHYLACTIC TRANSFUSION REACTION			
subjects affected / exposed	0 / 157 (0.00%)	0 / 22 (0.00%)	0 / 58 (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
LOWER LIMB FRACTURE			
subjects affected / exposed	1 / 157 (0.64%)	0 / 22 (0.00%)	1 / 58 (1.72%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INFUSION RELATED REACTION			

subjects affected / exposed	1 / 157 (0.64%)	0 / 22 (0.00%)	0 / 58 (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
FEMUR FRACTURE			
subjects affected / exposed	2 / 157 (1.27%)	0 / 22 (0.00%)	0 / 58 (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
FALL			
subjects affected / exposed	5 / 157 (3.18%)	0 / 22 (0.00%)	2 / 58 (3.45%)
occurrences causally related to treatment / all	0 / 5	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
ANKLE FRACTURE			
subjects affected / exposed	0 / 157 (0.00%)	0 / 22 (0.00%)	0 / 58 (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
OVERDOSE			
subjects affected / exposed	1 / 157 (0.64%)	0 / 22 (0.00%)	0 / 58 (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
SUBDURAL HAEMATOMA			
subjects affected / exposed	1 / 157 (0.64%)	0 / 22 (0.00%)	1 / 58 (1.72%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
POST PROCEDURAL HAEMORRHAGE			
subjects affected / exposed	1 / 157 (0.64%)	0 / 22 (0.00%)	0 / 58 (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
TRANSFUSION REACTION			
subjects affected / exposed	1 / 157 (0.64%)	0 / 22 (0.00%)	0 / 58 (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
SUBDURAL HAEMORRHAGE			

subjects affected / exposed	1 / 157 (0.64%)	0 / 22 (0.00%)	0 / 58 (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 disorders			
ACUTE CORONARY SYNDROME			
subjects affected / exposed	1 / 157 (0.64%)	0 / 22 (0.00%)	0 / 58 (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
ACUTE MYOCARDIAL INFARCTION			
subjects affected / exposed	0 / 157 (0.00%)	0 / 22 (0.00%)	1 / 58 (1.72%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
ANGINA PECTORIS			
subjects affected / exposed	0 / 157 (0.00%)	0 / 22 (0.00%)	0 / 58 (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
ATRIAL FIBRILLATION			
subjects affected / exposed	2 / 157 (1.27%)	0 / 22 (0.00%)	0 / 58 (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
ATRIAL FLUTTER			
subjects affected / exposed	1 / 157 (0.64%)	0 / 22 (0.00%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CARDIAC HYPERTROPHY			
subjects affected / exposed	1 / 157 (0.64%)	0 / 22 (0.00%)	0 / 58 (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 ARREST			
subjects affected / exposed	1 / 157 (0.64%)	0 / 22 (0.00%)	0 / 58 (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 FAILURE CONGESTIVE			

subjects affected / exposed	1 / 157 (0.64%)	0 / 22 (0.00%)	0 / 58 (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 FAILURE			
subjects affected / exposed	1 / 157 (0.64%)	0 / 22 (0.00%)	0 / 58 (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
BRADYCARDIA			
subjects affected / exposed	2 / 157 (1.27%)	0 / 22 (0.00%)	0 / 58 (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
SINUS BRADYCARDIA			
subjects affected / exposed	1 / 157 (0.64%)	0 / 22 (0.00%)	0 / 58 (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
PERICARDITIS			
subjects affected / exposed	1 / 157 (0.64%)	0 / 22 (0.00%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PERICARDIAL EFFUSION			
subjects affected / exposed	1 / 157 (0.64%)	0 / 22 (0.00%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CORONARY ARTERY DISEASE			
subjects affected / exposed	1 / 157 (0.64%)	0 / 22 (0.00%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CARDIOMYOPATHY			
subjects affected / exposed	1 / 157 (0.64%)	0 / 22 (0.00%)	0 / 58 (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
Nervous system disorders			
ATAXIA			

subjects affected / exposed	1 / 157 (0.64%)	0 / 22 (0.00%)	0 / 58 (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
BRAIN OEDEMA			
subjects affected / exposed	1 / 157 (0.64%)	0 / 22 (0.00%)	0 / 58 (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
CEREBRAL HAEMORRHAGE			
subjects affected / exposed	4 / 157 (2.55%)	0 / 22 (0.00%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 2	0 / 0	0 / 0
CEREBRAL INFARCTION			
subjects affected / exposed	0 / 157 (0.00%)	0 / 22 (0.00%)	1 / 58 (1.72%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ISCHAEMIC STROKE			
subjects affected / exposed	1 / 157 (0.64%)	0 / 22 (0.00%)	0 / 58 (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
HAEMORRHAGE INTRACRANIAL			
subjects affected / exposed	5 / 157 (3.18%)	0 / 22 (0.00%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	0 / 5	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 5	0 / 0	0 / 0
HEADACHE			
subjects affected / exposed	1 / 157 (0.64%)	0 / 22 (0.00%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INTRAVENTRICULAR HAEMORRHAGE			
subjects affected / exposed	1 / 157 (0.64%)	0 / 22 (0.00%)	0 / 58 (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
DYSARTHRIA			

subjects affected / exposed	1 / 157 (0.64%)	0 / 22 (0.00%)	0 / 58 (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
SYNCOPE			
subjects affected / exposed	4 / 157 (2.55%)	0 / 22 (0.00%)	1 / 58 (1.72%)
occurrences causally related to treatment / all	0 / 4	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NORMAL PRESSURE HYDROCEPHALUS			
subjects affected / exposed	1 / 157 (0.64%)	0 / 22 (0.00%)	0 / 58 (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
LUMBOSACRAL RADICULOPATHY			
subjects affected / exposed	1 / 157 (0.64%)	0 / 22 (0.00%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LOSS OF CONSCIOUSNESS			
subjects affected / exposed	1 / 157 (0.64%)	0 / 22 (0.00%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
FEBRILE NEUTROPENIA			
subjects affected / exposed	33 / 157 (21.02%)	5 / 22 (22.73%)	14 / 58 (24.14%)
occurrences causally related to treatment / all	4 / 44	0 / 5	4 / 20
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
AGRANULOCYTOSIS			
subjects affected / exposed	1 / 157 (0.64%)	0 / 22 (0.00%)	0 / 58 (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
ANAEMIA			
subjects affected / exposed	7 / 157 (4.46%)	0 / 22 (0.00%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	1 / 7	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FEBRILE BONE MARROW APLASIA			

subjects affected / exposed	3 / 157 (1.91%)	0 / 22 (0.00%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	0 / 5	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LEUKOSTASIS SYNDROME			
subjects affected / exposed	0 / 157 (0.00%)	0 / 22 (0.00%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NEUTROPENIA			
subjects affected / exposed	3 / 157 (1.91%)	0 / 22 (0.00%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	1 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
LEUKOCYTOSIS			
subjects affected / exposed	3 / 157 (1.91%)	0 / 22 (0.00%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 2	0 / 0	0 / 0
LEUKAEMOID REACTION			
subjects affected / exposed	1 / 157 (0.64%)	0 / 22 (0.00%)	0 / 58 (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
HYPERLEUKOCYTOSIS			
subjects affected / exposed	2 / 157 (1.27%)	1 / 22 (4.55%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
HAEMORRHAGIC DISORDER			
subjects affected / exposed	1 / 157 (0.64%)	0 / 22 (0.00%)	0 / 58 (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
PANCYTOPENIA			
subjects affected / exposed	4 / 157 (2.55%)	0 / 22 (0.00%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	1 / 4	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 2	0 / 0	0 / 0
THROMBOCYTOPENIA			

subjects affected / exposed	6 / 157 (3.82%)	0 / 22 (0.00%)	1 / 58 (1.72%)
occurrences causally related to treatment / all	3 / 7	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
RETINAL HAEMORRHAGE			
subjects affected / exposed	0 / 157 (0.00%)	0 / 22 (0.00%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
COLITIS			
subjects affected / exposed	1 / 157 (0.64%)	0 / 22 (0.00%)	1 / 58 (1.72%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ASCITES			
subjects affected / exposed	1 / 157 (0.64%)	0 / 22 (0.00%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ABDOMINAL PAIN			
subjects affected / exposed	1 / 157 (0.64%)	0 / 22 (0.00%)	0 / 58 (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
DIARRHOEA HAEMORRHAGIC			
subjects affected / exposed	1 / 157 (0.64%)	0 / 22 (0.00%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DIARRHOEA			
subjects affected / exposed	2 / 157 (1.27%)	0 / 22 (0.00%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CROHN'S DISEASE			
subjects affected / exposed	1 / 157 (0.64%)	0 / 22 (0.00%)	0 / 58 (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
CONSTIPATION			

subjects affected / exposed	1 / 157 (0.64%)	0 / 22 (0.00%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ENTEROCOLITIS			
subjects affected / exposed	1 / 157 (0.64%)	0 / 22 (0.00%)	0 / 58 (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
ENTEROCOLITIS HAEMORRHAGIC			
subjects affected / exposed	1 / 157 (0.64%)	0 / 22 (0.00%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GASTROINTESTINAL DISORDER			
subjects affected / exposed	1 / 157 (0.64%)	0 / 22 (0.00%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GASTROINTESTINAL HAEMORRHAGE			
subjects affected / exposed	1 / 157 (0.64%)	0 / 22 (0.00%)	1 / 58 (1.72%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MELAENA			
subjects affected / exposed	0 / 157 (0.00%)	0 / 22 (0.00%)	0 / 58 (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
LOWER GASTROINTESTINAL HAEMORRHAGE			
subjects affected / exposed	1 / 157 (0.64%)	0 / 22 (0.00%)	0 / 58 (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
INGUINAL HERNIA			
subjects affected / exposed	1 / 157 (0.64%)	0 / 22 (0.00%)	0 / 58 (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
GINGIVAL HYPERTROPHY			

subjects affected / exposed	1 / 157 (0.64%)	0 / 22 (0.00%)	0 / 58 (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
MOUTH HAEMORRHAGE			
subjects affected / exposed	2 / 157 (1.27%)	0 / 22 (0.00%)	0 / 58 (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
OESOPHAGITIS			
subjects affected / exposed	1 / 157 (0.64%)	0 / 22 (0.00%)	0 / 58 (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
OESOPHAGEAL ULCER			
subjects affected / exposed	1 / 157 (0.64%)	0 / 22 (0.00%)	0 / 58 (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
ODYNOPHAGIA			
subjects affected / exposed	1 / 157 (0.64%)	0 / 22 (0.00%)	0 / 58 (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
NAUSEA			
subjects affected / exposed	3 / 157 (1.91%)	0 / 22 (0.00%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ORAL BLOOD BLISTER			
subjects affected / exposed	1 / 157 (0.64%)	0 / 22 (0.00%)	0 / 58 (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 HAEMORRHAGE			
subjects affected / exposed	1 / 157 (0.64%)	0 / 22 (0.00%)	0 / 58 (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
STOMATITIS			

subjects affected / exposed	0 / 157 (0.00%)	0 / 22 (0.00%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VOMITING			
subjects affected / exposed	2 / 157 (1.27%)	0 / 22 (0.00%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
UPPER GASTROINTESTINAL HAEMORRHAGE			
subjects affected / exposed	1 / 157 (0.64%)	0 / 22 (0.00%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
CHOLANGITIS ACUTE			
subjects affected / exposed	1 / 157 (0.64%)	0 / 22 (0.00%)	0 / 58 (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
CHOLELITHIASIS MIGRATION			
subjects affected / exposed	1 / 157 (0.64%)	0 / 22 (0.00%)	0 / 58 (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 HEPATIC FAILURE			
subjects affected / exposed	1 / 157 (0.64%)	0 / 22 (0.00%)	0 / 58 (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
HEPATOTOXICITY			
subjects affected / exposed	0 / 157 (0.00%)	0 / 22 (0.00%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HEPATIC FAILURE			
subjects affected / exposed	1 / 157 (0.64%)	0 / 22 (0.00%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
HEPATIC CYTOLYSIS			

subjects affected / exposed	0 / 157 (0.00%)	0 / 22 (0.00%)	1 / 58 (1.72%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPERBILIRUBINAEMIA			
subjects affected / exposed	1 / 157 (0.64%)	0 / 22 (0.00%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
ECCHYMOSIS			
subjects affected / exposed	1 / 157 (0.64%)	0 / 22 (0.00%)	0 / 58 (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
PURPURA			
subjects affected / exposed	1 / 157 (0.64%)	0 / 22 (0.00%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RASH			
subjects affected / exposed	2 / 157 (1.27%)	0 / 22 (0.00%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
TOXIC SKIN ERUPTION			
subjects affected / exposed	1 / 157 (0.64%)	0 / 22 (0.00%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
RENAL COLIC			
subjects affected / exposed	1 / 157 (0.64%)	0 / 22 (0.00%)	0 / 58 (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
ACUTE KIDNEY INJURY			
subjects affected / exposed	4 / 157 (2.55%)	0 / 22 (0.00%)	3 / 58 (5.17%)
occurrences causally related to treatment / all	1 / 4	0 / 0	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HAEMATURIA			

subjects affected / exposed	0 / 157 (0.00%)	0 / 22 (0.00%)	1 / 58 (1.72%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
OLIGURIA			
subjects affected / exposed	0 / 157 (0.00%)	0 / 22 (0.00%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
URINARY RETENTION			
subjects affected / exposed	0 / 157 (0.00%)	1 / 22 (4.55%)	0 / 58 (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
RENAL IMPAIRMENT			
subjects affected / exposed	2 / 157 (1.27%)	0 / 22 (0.00%)	0 / 58 (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
RENAL FAILURE			
subjects affected / exposed	0 / 157 (0.00%)	0 / 22 (0.00%)	1 / 58 (1.72%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Musculoskeletal and connective tissue disorders			
ARTHRALGIA			
subjects affected / exposed	2 / 157 (1.27%)	0 / 22 (0.00%)	0 / 58 (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
BACK PAIN			
subjects affected / exposed	2 / 157 (1.27%)	0 / 22 (0.00%)	0 / 58 (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
BONE PAIN			
subjects affected / exposed	2 / 157 (1.27%)	0 / 22 (0.00%)	0 / 58 (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
JOINT EFFUSION			

subjects affected / exposed	1 / 157 (0.64%)	0 / 22 (0.00%)	0 / 58 (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
TENDONITIS			
subjects affected / exposed	1 / 157 (0.64%)	0 / 22 (0.00%)	0 / 58 (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
NECK PAIN			
subjects affected / exposed	1 / 157 (0.64%)	0 / 22 (0.00%)	0 / 58 (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
MUSCULAR WEAKNESS			
subjects affected / exposed	1 / 157 (0.64%)	0 / 22 (0.00%)	0 / 58 (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
PAIN IN EXTREMITY			
subjects affected / exposed	2 / 157 (1.27%)	0 / 22 (0.00%)	0 / 58 (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
Infections and infestations			
ACUTE SINUSITIS			
subjects affected / exposed	1 / 157 (0.64%)	0 / 22 (0.00%)	0 / 58 (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
ACARODERMATITIS			
subjects affected / exposed	0 / 157 (0.00%)	0 / 22 (0.00%)	1 / 58 (1.72%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ANAL ABSCESS			
subjects affected / exposed	0 / 157 (0.00%)	0 / 22 (0.00%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CLOSTRIDIAL SEPSIS			

subjects affected / exposed	1 / 157 (0.64%)	0 / 22 (0.00%)	0 / 58 (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
CELLULITIS			
subjects affected / exposed	1 / 157 (0.64%)	0 / 22 (0.00%)	1 / 58 (1.72%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CAMPYLOBACTER INFECTION			
subjects affected / exposed	1 / 157 (0.64%)	0 / 22 (0.00%)	0 / 58 (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
BRONCHOPULMONARY ASPERGILLOSIS			
subjects affected / exposed	0 / 157 (0.00%)	0 / 22 (0.00%)	2 / 58 (3.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BRONCHITIS			
subjects affected / exposed	0 / 157 (0.00%)	0 / 22 (0.00%)	0 / 58 (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
BREVIBACTERIUM INFECTION			
subjects affected / exposed	0 / 157 (0.00%)	0 / 22 (0.00%)	0 / 58 (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
BACTERAEMIA			
subjects affected / exposed	4 / 157 (2.55%)	0 / 22 (0.00%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
APPENDICITIS			
subjects affected / exposed	0 / 157 (0.00%)	0 / 22 (0.00%)	1 / 58 (1.72%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CLOSTRIDIUM DIFFICILE COLITIS			

subjects affected / exposed	4 / 157 (2.55%)	0 / 22 (0.00%)	1 / 58 (1.72%)
occurrences causally related to treatment / all	1 / 6	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 2	0 / 0	0 / 0
DEVICE RELATED INFECTION			
subjects affected / exposed	0 / 157 (0.00%)	0 / 22 (0.00%)	1 / 58 (1.72%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19 PNEUMONIA			
subjects affected / exposed	1 / 157 (0.64%)	0 / 22 (0.00%)	0 / 58 (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
CLOSTRIDIUM DIFFICILE INFECTION			
subjects affected / exposed	0 / 157 (0.00%)	0 / 22 (0.00%)	1 / 58 (1.72%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DISSEMINATED MUCORMYCOSIS			
subjects affected / exposed	1 / 157 (0.64%)	0 / 22 (0.00%)	0 / 58 (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
ESCHERICHIA SEPSIS			
subjects affected / exposed	1 / 157 (0.64%)	0 / 22 (0.00%)	0 / 58 (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
ENTEROCOLITIS INFECTIOUS			
subjects affected / exposed	1 / 157 (0.64%)	0 / 22 (0.00%)	0 / 58 (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
EPIGLOTTITIS			
subjects affected / exposed	0 / 157 (0.00%)	0 / 22 (0.00%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ESCHERICHIA BACTERAEMIA			

subjects affected / exposed	1 / 157 (0.64%)	1 / 22 (4.55%)	0 / 58 (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
ENTEROCOCCAL INFECTION			
subjects affected / exposed	1 / 157 (0.64%)	0 / 22 (0.00%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GASTROENTERITIS			
subjects affected / exposed	1 / 157 (0.64%)	0 / 22 (0.00%)	1 / 58 (1.72%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FURUNCLE			
subjects affected / exposed	0 / 157 (0.00%)	0 / 22 (0.00%)	1 / 58 (1.72%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ESCHERICHIA URINARY TRACT INFECTION			
subjects affected / exposed	2 / 157 (1.27%)	1 / 22 (4.55%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GASTROINTESTINAL INFECTION			
subjects affected / exposed	1 / 157 (0.64%)	0 / 22 (0.00%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HERPES SIMPLEX			
subjects affected / exposed	0 / 157 (0.00%)	0 / 22 (0.00%)	1 / 58 (1.72%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HEPATOSPLENIC CANDIDIASIS			
subjects affected / exposed	1 / 157 (0.64%)	0 / 22 (0.00%)	0 / 58 (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
HEPATIC INFECTION			

subjects affected / exposed	0 / 157 (0.00%)	0 / 22 (0.00%)	0 / 58 (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
GINGIVITIS			
subjects affected / exposed	1 / 157 (0.64%)	0 / 22 (0.00%)	0 / 58 (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
INFECTION			
subjects affected / exposed	4 / 157 (2.55%)	0 / 22 (0.00%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	1 / 4	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INFLUENZA			
subjects affected / exposed	2 / 157 (1.27%)	0 / 22 (0.00%)	0 / 58 (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
INJECTION SITE CELLULITIS			
subjects affected / exposed	0 / 157 (0.00%)	0 / 22 (0.00%)	1 / 58 (1.72%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INTERVERTEBRAL DISCITIS			
subjects affected / exposed	0 / 157 (0.00%)	0 / 22 (0.00%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MENINGITIS LISTERIA			
subjects affected / exposed	1 / 157 (0.64%)	0 / 22 (0.00%)	0 / 58 (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
LOCALISED INFECTION			
subjects affected / exposed	0 / 157 (0.00%)	1 / 22 (4.55%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
LIVER ABSCESS			

subjects affected / exposed	0 / 157 (0.00%)	0 / 22 (0.00%)	1 / 58 (1.72%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
KLEBSIELLA BACTERAEMIA			
subjects affected / exposed	1 / 157 (0.64%)	0 / 22 (0.00%)	0 / 58 (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
LOWER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	0 / 157 (0.00%)	0 / 22 (0.00%)	1 / 58 (1.72%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NEUTROPENIC SEPSIS			
subjects affected / exposed	3 / 157 (1.91%)	0 / 22 (0.00%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	1 / 4	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NOCARDIA SEPSIS			
subjects affected / exposed	1 / 157 (0.64%)	0 / 22 (0.00%)	0 / 58 (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
NOCARDIOSIS			
subjects affected / exposed	1 / 157 (0.64%)	0 / 22 (0.00%)	0 / 58 (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
OTITIS EXTERNA			
subjects affected / exposed	1 / 157 (0.64%)	0 / 22 (0.00%)	0 / 58 (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
PERIORBITAL CELLULITIS			
subjects affected / exposed	2 / 157 (1.27%)	0 / 22 (0.00%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PERIRECTAL ABSCESS			

subjects affected / exposed	1 / 157 (0.64%)	0 / 22 (0.00%)	1 / 58 (1.72%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PHARYNGITIS			
subjects affected / exposed	0 / 157 (0.00%)	0 / 22 (0.00%)	0 / 58 (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	27 / 157 (17.20%)	2 / 22 (9.09%)	8 / 58 (13.79%)
occurrences causally related to treatment / all	1 / 31	0 / 2	2 / 15
deaths causally related to treatment / all	0 / 6	0 / 1	0 / 2
PNEUMONIA INFLUENZAL			
subjects affected / exposed	1 / 157 (0.64%)	0 / 22 (0.00%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PNEUMONIA LEGIONELLA			
subjects affected / exposed	1 / 157 (0.64%)	0 / 22 (0.00%)	0 / 58 (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
PNEUMONIA RESPIRATORY SYNCYTIAL VIRAL			
subjects affected / exposed	1 / 157 (0.64%)	0 / 22 (0.00%)	0 / 58 (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
PNEUMONIA FUNGAL			
subjects affected / exposed	5 / 157 (3.18%)	0 / 22 (0.00%)	2 / 58 (3.45%)
occurrences causally related to treatment / all	0 / 8	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
PNEUMONIA BACTERIAL			
subjects affected / exposed	1 / 157 (0.64%)	0 / 22 (0.00%)	0 / 58 (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
PSEUDOMONAS INFECTION			

subjects affected / exposed	1 / 157 (0.64%)	0 / 22 (0.00%)	0 / 58 (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
PYELONEPHRITIS ACUTE			
subjects affected / exposed	1 / 157 (0.64%)	0 / 22 (0.00%)	0 / 58 (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 SYNCYTIAL VIRUS INFECTION			
subjects affected / exposed	1 / 157 (0.64%)	0 / 22 (0.00%)	0 / 58 (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
SEPTIC SHOCK			
subjects affected / exposed	6 / 157 (3.82%)	2 / 22 (9.09%)	1 / 58 (1.72%)
occurrences causally related to treatment / all	0 / 6	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 5	0 / 2	0 / 1
SEPSIS			
subjects affected / exposed	17 / 157 (10.83%)	0 / 22 (0.00%)	3 / 58 (5.17%)
occurrences causally related to treatment / all	0 / 21	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 10	0 / 0	0 / 2
RESPIRATORY TRACT INFECTION			
subjects affected / exposed	2 / 157 (1.27%)	0 / 22 (0.00%)	0 / 58 (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
SINUSITIS			
subjects affected / exposed	0 / 157 (0.00%)	0 / 22 (0.00%)	0 / 58 (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
STENOTROPHOMONAS INFECTION			
subjects affected / exposed	1 / 157 (0.64%)	0 / 22 (0.00%)	0 / 58 (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
STAPHYLOCOCCAL SEPSIS			

subjects affected / exposed	2 / 157 (1.27%)	0 / 22 (0.00%)	0 / 58 (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
STAPHYLOCOCCAL BACTERAEMIA			
subjects affected / exposed	1 / 157 (0.64%)	0 / 22 (0.00%)	0 / 58 (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
SKIN INFECTION			
subjects affected / exposed	1 / 157 (0.64%)	0 / 22 (0.00%)	2 / 58 (3.45%)
occurrences causally related to treatment / all	0 / 1	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SUBCUTANEOUS ABSCESS			
subjects affected / exposed	2 / 157 (1.27%)	0 / 22 (0.00%)	0 / 58 (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
TOOTH ABSCESS			
subjects affected / exposed	1 / 157 (0.64%)	0 / 22 (0.00%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	2 / 157 (1.27%)	0 / 22 (0.00%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VASCULAR DEVICE INFECTION			
subjects affected / exposed	1 / 157 (0.64%)	0 / 22 (0.00%)	0 / 58 (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
URINARY TRACT INFECTION ENTEROCOCCAL			
subjects affected / exposed	1 / 157 (0.64%)	0 / 22 (0.00%)	0 / 58 (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
URINARY TRACT INFECTION			

subjects affected / exposed	4 / 157 (2.55%)	1 / 22 (4.55%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
URETHRITIS			
subjects affected / exposed	0 / 157 (0.00%)	0 / 22 (0.00%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
DEHYDRATION			
subjects affected / exposed	5 / 157 (3.18%)	0 / 22 (0.00%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	0 / 5	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DECREASED APPETITE			
subjects affected / exposed	1 / 157 (0.64%)	0 / 22 (0.00%)	0 / 58 (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
DIABETIC METABOLIC DECOMPENSATION			
subjects affected / exposed	1 / 157 (0.64%)	0 / 22 (0.00%)	0 / 58 (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
TUMOUR LYSIS SYNDROME			
subjects affected / exposed	1 / 157 (0.64%)	0 / 22 (0.00%)	0 / 58 (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
HYPONATRAEMIA			
subjects affected / exposed	3 / 157 (1.91%)	0 / 22 (0.00%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	1 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPOKALAEMIA			
subjects affected / exposed	4 / 157 (2.55%)	0 / 22 (0.00%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPERGLYCAEMIA			

subjects affected / exposed	2 / 157 (1.27%)	0 / 22 (0.00%)	0 / 58 (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

Serious adverse events	LDAC + BSC	IDAC + BSC	
Total subjects affected by serious adverse events			
subjects affected / exposed	27 / 33 (81.82%)	17 / 28 (60.71%)	
number of deaths (all causes)	32	22	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
ACUTE LEUKAEMIA			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
GASTRIC CANCER			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ONCOLOGIC COMPLICATION			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
SQUAMOUS CELL CARCINOMA			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
SQUAMOUS CELL CARCINOMA OF SKIN			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ACUTE LYMPHOCYTIC LEUKAEMIA			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

ACUTE MYELOID LEUKAEMIA			
subjects affected / exposed	1 / 33 (3.03%)	1 / 28 (3.57%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
ACUTE MYELOID LEUKAEMIA RECURRENT			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
DIFFERENTIATION SYNDROME			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ENDOMETRIAL CANCER			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
HAEMORRHAGE			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
HYPOTENSION			
subjects affected / exposed	0 / 33 (0.00%)	1 / 28 (3.57%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
ASTHENIA			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
FATIGUE			

subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
GENERAL PHYSICAL HEALTH DETERIORATION			
subjects affected / exposed	1 / 33 (3.03%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PYREXIA			
subjects affected / exposed	3 / 33 (9.09%)	5 / 28 (17.86%)	
occurrences causally related to treatment / all	0 / 3	5 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
INFLUENZA LIKE ILLNESS			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
MALAISE			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
MUCOSAL INFLAMMATION			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
MULTIPLE ORGAN DYSFUNCTION SYNDROME			
subjects affected / exposed	0 / 33 (0.00%)	1 / 28 (3.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
ORGAN FAILURE			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PHYSICAL DECONDITIONING			

subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
GRAFT VERSUS HOST DISEASE			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
BENIGN PROSTATIC HYPERPLASIA			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
ACUTE RESPIRATORY FAILURE			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
CHRONIC OBSTRUCTIVE PULMONARY DISEASE			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
LUNG INFILTRATION			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
LUNG DISORDER			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
EPISTAXIS			

subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
DYSPNOEA			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ORGANISING PNEUMONIA			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PLEURAL EFFUSION			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PNEUMONITIS			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
RESPIRATORY DISTRESS			
subjects affected / exposed	1 / 33 (3.03%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
RESPIRATORY FAILURE			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
CONFUSIONAL STATE			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			

BLAST CELL COUNT INCREASED			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ALANINE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
LIVER FUNCTION TEST INCREASED			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
BLOOD CREATININE INCREASED			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
EJECTION FRACTION DECREASED			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
GENERAL PHYSICAL CONDITION ABNORMAL			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
BLOOD BILIRUBIN INCREASED			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
TRANSAMINASES INCREASED			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PLATELET COUNT DECREASED			

subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
ANAPHYLACTIC TRANSFUSION REACTION			
subjects affected / exposed	1 / 33 (3.03%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
LOWER LIMB FRACTURE			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
INFUSION RELATED REACTION			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
FEMUR FRACTURE			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
FALL			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ANKLE FRACTURE			
subjects affected / exposed	0 / 33 (0.00%)	2 / 28 (7.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
OVERDOSE			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
SUBDURAL HAEMATOMA			

subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
POST PROCEDURAL HAEMORRHAGE			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
TRANSFUSION REACTION			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
SUBDURAL HAEMORRHAGE			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
ACUTE CORONARY SYNDROME			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ACUTE MYOCARDIAL INFARCTION			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ANGINA PECTORIS			
subjects affected / exposed	1 / 33 (3.03%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ATRIAL FIBRILLATION			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ATRIAL FLUTTER			

subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
CARDIAC HYPERTROPHY			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
CARDIAC ARREST			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
CARDIAC FAILURE CONGESTIVE			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
CARDIAC FAILURE			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
BRADYCARDIA			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
SINUS BRADYCARDIA			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PERICARDITIS			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PERICARDIAL EFFUSION			

subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
CORONARY ARTERY DISEASE			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
CARDIOMYOPATHY			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
ATAXIA			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
BRAIN OEDEMA			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
CEREBRAL HAEMORRHAGE			
subjects affected / exposed	1 / 33 (3.03%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
CEREBRAL INFARCTION			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ISCHAEMIC STROKE			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
HAEMORRHAGE INTRACRANIAL			

subjects affected / exposed	1 / 33 (3.03%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
HEADACHE			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
INTRAVENTRICULAR HAEMORRHAGE			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
DYSARTHRIA			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
SYNCOPE			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
NORMAL PRESSURE HYDROCEPHALUS			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
LUMBOSACRAL RADICULOPATHY			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
LOSS OF CONSCIOUSNESS			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
FEBRILE NEUTROPENIA			

subjects affected / exposed	13 / 33 (39.39%)	7 / 28 (25.00%)	
occurrences causally related to treatment / all	3 / 15	6 / 9	
deaths causally related to treatment / all	1 / 2	0 / 0	
AGRANULOCYTOSIS			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ANAEMIA			
subjects affected / exposed	1 / 33 (3.03%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
FEBRILE BONE MARROW APLASIA			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
LEUKOSTASIS SYNDROME			
subjects affected / exposed	1 / 33 (3.03%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
NEUTROPENIA			
subjects affected / exposed	0 / 33 (0.00%)	1 / 28 (3.57%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
LEUKOCYTOSIS			
subjects affected / exposed	1 / 33 (3.03%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
LEUKAEMOID REACTION			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
HYPERLEUKOCYTOSIS			

subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
HAEMORRHAGIC DISORDER			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PANCYTOPENIA			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
THROMBOCYTOPENIA			
subjects affected / exposed	1 / 33 (3.03%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
RETINAL HAEMORRHAGE			
subjects affected / exposed	1 / 33 (3.03%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
COLITIS			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ASCITES			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ABDOMINAL PAIN			
subjects affected / exposed	1 / 33 (3.03%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
DIARRHOEA HAEMORRHAGIC			

subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
DIARRHOEA			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
CROHN'S DISEASE			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
CONSTIPATION			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ENTEROCOLITIS			
subjects affected / exposed	0 / 33 (0.00%)	1 / 28 (3.57%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
ENTEROCOLITIS HAEMORRHAGIC			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
GASTROINTESTINAL DISORDER			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
GASTROINTESTINAL HAEMORRHAGE			
subjects affected / exposed	1 / 33 (3.03%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
MELAENA			

subjects affected / exposed	1 / 33 (3.03%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
LOWER GASTROINTESTINAL HAEMORRHAGE			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
INGUINAL HERNIA			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
GINGIVAL HYPERTROPHY			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
MOUTH HAEMORRHAGE			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
OESOPHAGITIS			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
OESOPHAGEAL ULCER			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ODYNOPHAGIA			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
NAUSEA			

subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ORAL BLOOD BLISTER			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
RECTAL HAEMORRHAGE			
subjects affected / exposed	0 / 33 (0.00%)	1 / 28 (3.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
STOMATITIS			
subjects affected / exposed	1 / 33 (3.03%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
VOMITING			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
UPPER GASTROINTESTINAL HAEMORRHAGE			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
CHOLANGITIS ACUTE			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
CHOLELITHIASIS MIGRATION			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
CHRONIC HEPATIC FAILURE			

subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
HEPATOTOXICITY			
subjects affected / exposed	1 / 33 (3.03%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
HEPATIC FAILURE			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
HEPATIC CYTOLYSIS			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
HYPERBILIRUBINAEMIA			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
ECCHYMOSIS			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PURPURA			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
RASH			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
TOXIC SKIN ERUPTION			

subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
RENAL COLIC			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ACUTE KIDNEY INJURY			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
HAEMATURIA			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
OLIGURIA			
subjects affected / exposed	0 / 33 (0.00%)	1 / 28 (3.57%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
URINARY RETENTION			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
RENAL IMPAIRMENT			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
RENAL FAILURE			
subjects affected / exposed	0 / 33 (0.00%)	1 / 28 (3.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Musculoskeletal and connective tissue disorders			

ARTHRALGIA			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
BACK PAIN			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
BONE PAIN			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
JOINT EFFUSION			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
TENDONITIS			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
NECK PAIN			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
MUSCULAR WEAKNESS			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PAIN IN EXTREMITY			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			

ACUTE SINUSITIS			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ACARODERMATITIS			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ANAL ABSCESS			
subjects affected / exposed	1 / 33 (3.03%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
CLOSTRIDIAL SEPSIS			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
CELLULITIS			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
CAMPYLOBACTER INFECTION			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
BRONCHOPULMONARY ASPERGILLOSIS			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
BRONCHITIS			
subjects affected / exposed	1 / 33 (3.03%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
BREVIBACTERIUM INFECTION			

subjects affected / exposed	0 / 33 (0.00%)	1 / 28 (3.57%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
BACTERAEMIA			
subjects affected / exposed	1 / 33 (3.03%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
APPENDICITIS			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
CLOSTRIDIUM DIFFICILE COLITIS			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
DEVICE RELATED INFECTION			
subjects affected / exposed	1 / 33 (3.03%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19 PNEUMONIA			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
CLOSTRIDIUM DIFFICILE INFECTION			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
DISSEMINATED MUCORMYCOSIS			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ESCHERICHIA SEPSIS			

subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ENTEROCOLITIS INFECTIOUS			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
EPIGLOTTITIS			
subjects affected / exposed	0 / 33 (0.00%)	1 / 28 (3.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
ESCHERICHIA BACTERAEMIA			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ENTEROCOCCAL INFECTION			
subjects affected / exposed	1 / 33 (3.03%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
GASTROENTERITIS			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
FURUNCLE			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ESCHERICHIA URINARY TRACT INFECTION			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
GASTROINTESTINAL INFECTION			

subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
HERPES SIMPLEX			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
HEPATOSPLENIC CANDIDIASIS			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
HEPATIC INFECTION			
subjects affected / exposed	1 / 33 (3.03%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
GINGIVITIS			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
INFECTION			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
INFLUENZA			
subjects affected / exposed	1 / 33 (3.03%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
INJECTION SITE CELLULITIS			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
INTERVERTEBRAL DISCITIS			

subjects affected / exposed	1 / 33 (3.03%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
MENINGITIS LISTERIA			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
LOCALISED INFECTION			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
LIVER ABSCESS			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
KLEBSIELLA BACTERAEMIA			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
LOWER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
NEUTROPENIC SEPSIS			
subjects affected / exposed	1 / 33 (3.03%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
NOCARDIA SEPSIS			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
NOCARDIOSIS			

subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
OTITIS EXTERNA			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PERIORBITAL CELLULITIS			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PERIRECTAL ABSCESS			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PHARYNGITIS			
subjects affected / exposed	1 / 33 (3.03%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PNEUMONIA			
subjects affected / exposed	4 / 33 (12.12%)	3 / 28 (10.71%)	
occurrences causally related to treatment / all	1 / 4	3 / 3	
deaths causally related to treatment / all	0 / 0	1 / 1	
PNEUMONIA INFLUENZAL			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PNEUMONIA LEGIONELLA			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PNEUMONIA RESPIRATORY SYNCYTIAL VIRAL			

subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PNEUMONIA FUNGAL			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PNEUMONIA BACTERIAL			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PSEUDOMONAS INFECTION			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PYELONEPHRITIS ACUTE			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
RESPIRATORY SYNCYTIAL VIRUS INFECTION			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
SEPTIC SHOCK			
subjects affected / exposed	0 / 33 (0.00%)	1 / 28 (3.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
SEPSIS			
subjects affected / exposed	2 / 33 (6.06%)	1 / 28 (3.57%)	
occurrences causally related to treatment / all	0 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
RESPIRATORY TRACT INFECTION			

subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
SINUSITIS			
subjects affected / exposed	1 / 33 (3.03%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
STENOTROPHOMONAS INFECTION			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
STAPHYLOCOCCAL SEPSIS			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
STAPHYLOCOCCAL BACTERAEMIA			
subjects affected / exposed	1 / 33 (3.03%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
SKIN INFECTION			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
SUBCUTANEOUS ABSCESS			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
TOOTH ABSCESS			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
UPPER RESPIRATORY TRACT INFECTION			

subjects affected / exposed	0 / 33 (0.00%)	1 / 28 (3.57%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
VASCULAR DEVICE INFECTION			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
URINARY TRACT INFECTION ENTEROCOCCAL			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
URINARY TRACT INFECTION			
subjects affected / exposed	1 / 33 (3.03%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
URETHRITIS			
subjects affected / exposed	0 / 33 (0.00%)	1 / 28 (3.57%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
DEHYDRATION			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
DECREASED APPETITE			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
DIABETIC METABOLIC DECOMPENSATION			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
TUMOUR LYSIS SYNDROME			

subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
HYPONATRAEMIA			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
HYPOKALAEMIA			
subjects affected / exposed	1 / 33 (3.03%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
HYPERGLYCAEMIA			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	AG-221	BSC Only	Azacitidine + BSC
Total subjects affected by non-serious adverse events			
subjects affected / exposed	154 / 157 (98.09%)	11 / 22 (50.00%)	52 / 58 (89.66%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
DIFFERENTIATION SYNDROME			
subjects affected / exposed	16 / 157 (10.19%)	0 / 22 (0.00%)	0 / 58 (0.00%)
occurrences (all)	17	0	0
Vascular disorders			
HYPOTENSION			
subjects affected / exposed	15 / 157 (9.55%)	0 / 22 (0.00%)	1 / 58 (1.72%)
occurrences (all)	20	0	1
HYPERTENSION			
subjects affected / exposed	8 / 157 (5.10%)	0 / 22 (0.00%)	4 / 58 (6.90%)
occurrences (all)	13	0	4
HAEMATOMA			

subjects affected / exposed	11 / 157 (7.01%)	0 / 22 (0.00%)	2 / 58 (3.45%)
occurrences (all)	12	0	2
PHLEBITIS			
subjects affected / exposed	2 / 157 (1.27%)	1 / 22 (4.55%)	3 / 58 (5.17%)
occurrences (all)	2	1	3
General disorders and administration site conditions			
INJECTION SITE PAIN			
subjects affected / exposed	0 / 157 (0.00%)	0 / 22 (0.00%)	6 / 58 (10.34%)
occurrences (all)	0	0	9
INFLUENZA LIKE ILLNESS			
subjects affected / exposed	5 / 157 (3.18%)	0 / 22 (0.00%)	3 / 58 (5.17%)
occurrences (all)	5	0	4
GENERAL PHYSICAL HEALTH DETERIORATION			
subjects affected / exposed	10 / 157 (6.37%)	1 / 22 (4.55%)	0 / 58 (0.00%)
occurrences (all)	12	1	0
FATIGUE			
subjects affected / exposed	45 / 157 (28.66%)	0 / 22 (0.00%)	10 / 58 (17.24%)
occurrences (all)	61	0	10
ASTHENIA			
subjects affected / exposed	29 / 157 (18.47%)	2 / 22 (9.09%)	13 / 58 (22.41%)
occurrences (all)	32	2	17
NON-CARDIAC CHEST PAIN			
subjects affected / exposed	5 / 157 (3.18%)	1 / 22 (4.55%)	3 / 58 (5.17%)
occurrences (all)	7	1	3
PYREXIA			
subjects affected / exposed	37 / 157 (23.57%)	4 / 22 (18.18%)	14 / 58 (24.14%)
occurrences (all)	51	4	17
OEDEMA PERIPHERAL			
subjects affected / exposed	33 / 157 (21.02%)	1 / 22 (4.55%)	13 / 58 (22.41%)
occurrences (all)	43	1	18
Reproductive system and breast disorders			
VAGINAL HAEMORRHAGE			
subjects affected / exposed	1 / 157 (0.64%)	0 / 22 (0.00%)	1 / 58 (1.72%)
occurrences (all)	1	0	1
Respiratory, thoracic and mediastinal			

disorders			
PLEURAL EFFUSION			
subjects affected / exposed	8 / 157 (5.10%)	1 / 22 (4.55%)	3 / 58 (5.17%)
occurrences (all)	8	1	3
OROPHARYNGEAL PAIN			
subjects affected / exposed	8 / 157 (5.10%)	0 / 22 (0.00%)	2 / 58 (3.45%)
occurrences (all)	9	0	3
EPISTAXIS			
subjects affected / exposed	27 / 157 (17.20%)	3 / 22 (13.64%)	10 / 58 (17.24%)
occurrences (all)	35	3	15
DYSPNOEA			
subjects affected / exposed	34 / 157 (21.66%)	2 / 22 (9.09%)	3 / 58 (5.17%)
occurrences (all)	51	2	4
COUGH			
subjects affected / exposed	27 / 157 (17.20%)	3 / 22 (13.64%)	9 / 58 (15.52%)
occurrences (all)	37	3	10
Psychiatric disorders			
CONFUSIONAL STATE			
subjects affected / exposed	9 / 157 (5.73%)	0 / 22 (0.00%)	0 / 58 (0.00%)
occurrences (all)	12	0	0
ANXIETY			
subjects affected / exposed	9 / 157 (5.73%)	0 / 22 (0.00%)	0 / 58 (0.00%)
occurrences (all)	9	0	0
DEPRESSION			
subjects affected / exposed	8 / 157 (5.10%)	0 / 22 (0.00%)	1 / 58 (1.72%)
occurrences (all)	8	0	1
INSOMNIA			
subjects affected / exposed	24 / 157 (15.29%)	1 / 22 (4.55%)	10 / 58 (17.24%)
occurrences (all)	26	1	17
Investigations			
ALANINE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	8 / 157 (5.10%)	0 / 22 (0.00%)	3 / 58 (5.17%)
occurrences (all)	9	0	3
ASPARTATE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	6 / 157 (3.82%)	0 / 22 (0.00%)	1 / 58 (1.72%)
occurrences (all)	6	0	1

BLOOD ALKALINE PHOSPHATASE INCREASED			
subjects affected / exposed	5 / 157 (3.18%)	0 / 22 (0.00%)	3 / 58 (5.17%)
occurrences (all)	10	0	4
BLOOD BILIRUBIN INCREASED			
subjects affected / exposed	41 / 157 (26.11%)	0 / 22 (0.00%)	1 / 58 (1.72%)
occurrences (all)	67	0	1
BLOOD CREATININE INCREASED			
subjects affected / exposed	20 / 157 (12.74%)	0 / 22 (0.00%)	5 / 58 (8.62%)
occurrences (all)	33	0	7
C-REACTIVE PROTEIN INCREASED			
subjects affected / exposed	8 / 157 (5.10%)	0 / 22 (0.00%)	4 / 58 (6.90%)
occurrences (all)	9	0	4
ELECTROCARDIOGRAM QT PROLONGED			
subjects affected / exposed	8 / 157 (5.10%)	0 / 22 (0.00%)	3 / 58 (5.17%)
occurrences (all)	9	0	3
WEIGHT DECREASED			
subjects affected / exposed	14 / 157 (8.92%)	0 / 22 (0.00%)	4 / 58 (6.90%)
occurrences (all)	16	0	5
WEIGHT INCREASED			
subjects affected / exposed	0 / 157 (0.00%)	0 / 22 (0.00%)	0 / 58 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
CONTUSION			
subjects affected / exposed	12 / 157 (7.64%)	0 / 22 (0.00%)	3 / 58 (5.17%)
occurrences (all)	13	0	3
FALL			
subjects affected / exposed	13 / 157 (8.28%)	0 / 22 (0.00%)	4 / 58 (6.90%)
occurrences (all)	15	0	4
Cardiac disorders			
TACHYCARDIA			
subjects affected / exposed	2 / 157 (1.27%)	2 / 22 (9.09%)	1 / 58 (1.72%)
occurrences (all)	3	2	1
Nervous system disorders			
HEADACHE			

subjects affected / exposed	24 / 157 (15.29%)	0 / 22 (0.00%)	3 / 58 (5.17%)
occurrences (all)	28	0	4
DIZZINESS			
subjects affected / exposed	23 / 157 (14.65%)	0 / 22 (0.00%)	0 / 58 (0.00%)
occurrences (all)	28	0	0
DYSGEUSIA			
subjects affected / exposed	12 / 157 (7.64%)	0 / 22 (0.00%)	0 / 58 (0.00%)
occurrences (all)	14	0	0
PERIPHERAL SENSORY NEUROPATHY			
subjects affected / exposed	4 / 157 (2.55%)	0 / 22 (0.00%)	3 / 58 (5.17%)
occurrences (all)	4	0	3
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	46 / 157 (29.30%)	2 / 22 (9.09%)	7 / 58 (12.07%)
occurrences (all)	83	2	13
FEBRILE NEUTROPENIA			
subjects affected / exposed	14 / 157 (8.92%)	0 / 22 (0.00%)	7 / 58 (12.07%)
occurrences (all)	17	0	12
LEUKOCYTOSIS			
subjects affected / exposed	20 / 157 (12.74%)	2 / 22 (9.09%)	3 / 58 (5.17%)
occurrences (all)	29	2	3
LEUKOPENIA			
subjects affected / exposed	13 / 157 (8.28%)	0 / 22 (0.00%)	3 / 58 (5.17%)
occurrences (all)	20	0	9
THROMBOCYTOPENIA			
subjects affected / exposed	48 / 157 (30.57%)	2 / 22 (9.09%)	17 / 58 (29.31%)
occurrences (all)	71	2	26
NEUTROPENIA			
subjects affected / exposed	29 / 157 (18.47%)	2 / 22 (9.09%)	14 / 58 (24.14%)
occurrences (all)	41	2	33
Eye disorders			
DRY EYE			
subjects affected / exposed	4 / 157 (2.55%)	0 / 22 (0.00%)	4 / 58 (6.90%)
occurrences (all)	4	0	4
CONJUNCTIVAL HAEMORRHAGE			

subjects affected / exposed	4 / 157 (2.55%)	0 / 22 (0.00%)	1 / 58 (1.72%)
occurrences (all)	4	0	2
Gastrointestinal disorders			
ABDOMINAL DISTENSION			
subjects affected / exposed	10 / 157 (6.37%)	0 / 22 (0.00%)	0 / 58 (0.00%)
occurrences (all)	13	0	0
ABDOMINAL PAIN			
subjects affected / exposed	17 / 157 (10.83%)	0 / 22 (0.00%)	5 / 58 (8.62%)
occurrences (all)	21	0	6
ABDOMINAL PAIN UPPER			
subjects affected / exposed	11 / 157 (7.01%)	2 / 22 (9.09%)	4 / 58 (6.90%)
occurrences (all)	16	2	5
CONSTIPATION			
subjects affected / exposed	30 / 157 (19.11%)	2 / 22 (9.09%)	23 / 58 (39.66%)
occurrences (all)	41	2	30
DIARRHOEA			
subjects affected / exposed	62 / 157 (39.49%)	0 / 22 (0.00%)	14 / 58 (24.14%)
occurrences (all)	86	0	15
DRY MOUTH			
subjects affected / exposed	2 / 157 (1.27%)	0 / 22 (0.00%)	3 / 58 (5.17%)
occurrences (all)	2	0	3
NAUSEA			
subjects affected / exposed	69 / 157 (43.95%)	2 / 22 (9.09%)	16 / 58 (27.59%)
occurrences (all)	90	2	27
MOUTH HAEMORRHAGE			
subjects affected / exposed	10 / 157 (6.37%)	1 / 22 (4.55%)	3 / 58 (5.17%)
occurrences (all)	12	1	6
MELAENA			
subjects affected / exposed	1 / 157 (0.64%)	0 / 22 (0.00%)	0 / 58 (0.00%)
occurrences (all)	1	0	0
HAEMORRHOIDS			
subjects affected / exposed	5 / 157 (3.18%)	1 / 22 (4.55%)	5 / 58 (8.62%)
occurrences (all)	5	1	6
GINGIVAL BLEEDING			
subjects affected / exposed	11 / 157 (7.01%)	1 / 22 (4.55%)	2 / 58 (3.45%)
occurrences (all)	11	1	2

DYSPEPSIA			
subjects affected / exposed	9 / 157 (5.73%)	1 / 22 (4.55%)	1 / 58 (1.72%)
occurrences (all)	10	1	1
STOMATITIS			
subjects affected / exposed	15 / 157 (9.55%)	1 / 22 (4.55%)	4 / 58 (6.90%)
occurrences (all)	19	1	7
VOMITING			
subjects affected / exposed	40 / 157 (25.48%)	1 / 22 (4.55%)	9 / 58 (15.52%)
occurrences (all)	56	1	15
Hepatobiliary disorders			
HYPERBILIRUBINAEMIA			
subjects affected / exposed	15 / 157 (9.55%)	0 / 22 (0.00%)	1 / 58 (1.72%)
occurrences (all)	18	0	1
Skin and subcutaneous tissue disorders			
ERYTHEMA			
subjects affected / exposed	6 / 157 (3.82%)	0 / 22 (0.00%)	5 / 58 (8.62%)
occurrences (all)	6	0	5
RASH MACULO-PAPULAR			
subjects affected / exposed	9 / 157 (5.73%)	0 / 22 (0.00%)	1 / 58 (1.72%)
occurrences (all)	10	0	1
RASH			
subjects affected / exposed	11 / 157 (7.01%)	0 / 22 (0.00%)	6 / 58 (10.34%)
occurrences (all)	13	0	7
PRURITUS			
subjects affected / exposed	13 / 157 (8.28%)	0 / 22 (0.00%)	0 / 58 (0.00%)
occurrences (all)	14	0	0
PETECHIAE			
subjects affected / exposed	13 / 157 (8.28%)	0 / 22 (0.00%)	4 / 58 (6.90%)
occurrences (all)	14	0	4
Renal and urinary disorders			
CHRONIC KIDNEY DISEASE			
subjects affected / exposed	2 / 157 (1.27%)	0 / 22 (0.00%)	3 / 58 (5.17%)
occurrences (all)	2	0	3
DYSURIA			
subjects affected / exposed	2 / 157 (1.27%)	0 / 22 (0.00%)	3 / 58 (5.17%)
occurrences (all)	2	0	3
Musculoskeletal and connective tissue			

disorders			
ARTHRALGIA			
subjects affected / exposed	13 / 157 (8.28%)	1 / 22 (4.55%)	0 / 58 (0.00%)
occurrences (all)	15	1	0
BACK PAIN			
subjects affected / exposed	21 / 157 (13.38%)	0 / 22 (0.00%)	3 / 58 (5.17%)
occurrences (all)	23	0	3
MUSCULAR WEAKNESS			
subjects affected / exposed	11 / 157 (7.01%)	1 / 22 (4.55%)	0 / 58 (0.00%)
occurrences (all)	13	1	0
PAIN IN EXTREMITY			
subjects affected / exposed	20 / 157 (12.74%)	0 / 22 (0.00%)	6 / 58 (10.34%)
occurrences (all)	26	0	6
Infections and infestations			
URINARY TRACT INFECTION			
subjects affected / exposed	12 / 157 (7.64%)	2 / 22 (9.09%)	1 / 58 (1.72%)
occurrences (all)	19	2	1
BRONCHITIS			
subjects affected / exposed	3 / 157 (1.91%)	0 / 22 (0.00%)	0 / 58 (0.00%)
occurrences (all)	3	0	0
CELLULITIS			
subjects affected / exposed	3 / 157 (1.91%)	1 / 22 (4.55%)	2 / 58 (3.45%)
occurrences (all)	5	1	2
INFECTION			
subjects affected / exposed	2 / 157 (1.27%)	0 / 22 (0.00%)	1 / 58 (1.72%)
occurrences (all)	2	0	1
ORAL CANDIDIASIS			
subjects affected / exposed	10 / 157 (6.37%)	1 / 22 (4.55%)	2 / 58 (3.45%)
occurrences (all)	13	1	2
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	13 / 157 (8.28%)	0 / 22 (0.00%)	6 / 58 (10.34%)
occurrences (all)	15	0	12
TOOTH INFECTION			
subjects affected / exposed	2 / 157 (1.27%)	0 / 22 (0.00%)	0 / 58 (0.00%)
occurrences (all)	2	0	0
RHINITIS			

subjects affected / exposed	4 / 157 (2.55%)	0 / 22 (0.00%)	3 / 58 (5.17%)
occurrences (all)	4	0	3
PNEUMONIA FUNGAL			
subjects affected / exposed	3 / 157 (1.91%)	0 / 22 (0.00%)	3 / 58 (5.17%)
occurrences (all)	3	0	3
PNEUMONIA			
subjects affected / exposed	13 / 157 (8.28%)	1 / 22 (4.55%)	7 / 58 (12.07%)
occurrences (all)	17	1	9
PHARYNGITIS			
subjects affected / exposed	3 / 157 (1.91%)	0 / 22 (0.00%)	0 / 58 (0.00%)
occurrences (all)	3	0	0
Metabolism and nutrition disorders			
DECREASED APPETITE			
subjects affected / exposed	49 / 157 (31.21%)	1 / 22 (4.55%)	13 / 58 (22.41%)
occurrences (all)	62	1	15
HYPERGLYCAEMIA			
subjects affected / exposed	11 / 157 (7.01%)	0 / 22 (0.00%)	1 / 58 (1.72%)
occurrences (all)	18	0	6
HYPERKALAEMIA			
subjects affected / exposed	2 / 157 (1.27%)	0 / 22 (0.00%)	3 / 58 (5.17%)
occurrences (all)	2	0	3
HYPOCALCAEMIA			
subjects affected / exposed	15 / 157 (9.55%)	0 / 22 (0.00%)	3 / 58 (5.17%)
occurrences (all)	17	0	3
HYPERURICAEMIA			
subjects affected / exposed	17 / 157 (10.83%)	0 / 22 (0.00%)	1 / 58 (1.72%)
occurrences (all)	24	0	1
HYPOKALAEMIA			
subjects affected / exposed	52 / 157 (33.12%)	1 / 22 (4.55%)	10 / 58 (17.24%)
occurrences (all)	73	1	15
HYPOMAGNESAEMIA			
subjects affected / exposed	19 / 157 (12.10%)	1 / 22 (4.55%)	3 / 58 (5.17%)
occurrences (all)	22	1	5
HYPONATRAEMIA			
subjects affected / exposed	10 / 157 (6.37%)	0 / 22 (0.00%)	2 / 58 (3.45%)
occurrences (all)	11	0	10

HYPOPHOSPHATAEMIA			
subjects affected / exposed	9 / 157 (5.73%)	0 / 22 (0.00%)	3 / 58 (5.17%)
occurrences (all)	10	0	5
HYPOALBUMINAEMIA			
subjects affected / exposed	13 / 157 (8.28%)	2 / 22 (9.09%)	4 / 58 (6.90%)
occurrences (all)	14	2	10

Non-serious adverse events	LDAC + BSC	IDAC + BSC	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	30 / 33 (90.91%)	24 / 28 (85.71%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
DIFFERENTIATION SYNDROME			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences (all)	0	0	
Vascular disorders			
HYPOTENSION			
subjects affected / exposed	0 / 33 (0.00%)	1 / 28 (3.57%)	
occurrences (all)	0	1	
HYPERTENSION			
subjects affected / exposed	1 / 33 (3.03%)	2 / 28 (7.14%)	
occurrences (all)	1	2	
HAEMATOMA			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences (all)	0	0	
PHLEBITIS			
subjects affected / exposed	0 / 33 (0.00%)	1 / 28 (3.57%)	
occurrences (all)	0	1	
General disorders and administration site conditions			
INJECTION SITE PAIN			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences (all)	0	0	
INFLUENZA LIKE ILLNESS			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences (all)	0	0	
GENERAL PHYSICAL HEALTH DETERIORATION			

subjects affected / exposed	0 / 33 (0.00%)	1 / 28 (3.57%)	
occurrences (all)	0	1	
FATIGUE			
subjects affected / exposed	6 / 33 (18.18%)	4 / 28 (14.29%)	
occurrences (all)	6	4	
ASTHENIA			
subjects affected / exposed	5 / 33 (15.15%)	4 / 28 (14.29%)	
occurrences (all)	8	4	
NON-CARDIAC CHEST PAIN			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences (all)	0	0	
PYREXIA			
subjects affected / exposed	5 / 33 (15.15%)	5 / 28 (17.86%)	
occurrences (all)	6	6	
OEDEMA PERIPHERAL			
subjects affected / exposed	6 / 33 (18.18%)	2 / 28 (7.14%)	
occurrences (all)	6	4	
Reproductive system and breast disorders			
VAGINAL HAEMORRHAGE			
subjects affected / exposed	0 / 33 (0.00%)	2 / 28 (7.14%)	
occurrences (all)	0	2	
Respiratory, thoracic and mediastinal disorders			
PLEURAL EFFUSION			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences (all)	0	0	
OROPHARYNGEAL PAIN			
subjects affected / exposed	4 / 33 (12.12%)	2 / 28 (7.14%)	
occurrences (all)	5	2	
EPISTAXIS			
subjects affected / exposed	4 / 33 (12.12%)	4 / 28 (14.29%)	
occurrences (all)	4	5	
DYSPNOEA			
subjects affected / exposed	3 / 33 (9.09%)	1 / 28 (3.57%)	
occurrences (all)	5	1	
COUGH			

subjects affected / exposed	8 / 33 (24.24%)	2 / 28 (7.14%)	
occurrences (all)	10	2	
Psychiatric disorders			
CONFUSIONAL STATE			
subjects affected / exposed	2 / 33 (6.06%)	2 / 28 (7.14%)	
occurrences (all)	2	2	
ANXIETY			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences (all)	0	0	
DEPRESSION			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences (all)	0	0	
INSOMNIA			
subjects affected / exposed	2 / 33 (6.06%)	2 / 28 (7.14%)	
occurrences (all)	2	2	
Investigations			
ALANINE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	2 / 33 (6.06%)	2 / 28 (7.14%)	
occurrences (all)	2	2	
ASPARTATE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	1 / 33 (3.03%)	2 / 28 (7.14%)	
occurrences (all)	1	2	
BLOOD ALKALINE PHOSPHATASE INCREASED			
subjects affected / exposed	0 / 33 (0.00%)	1 / 28 (3.57%)	
occurrences (all)	0	1	
BLOOD BILIRUBIN INCREASED			
subjects affected / exposed	1 / 33 (3.03%)	2 / 28 (7.14%)	
occurrences (all)	1	2	
BLOOD CREATININE INCREASED			
subjects affected / exposed	0 / 33 (0.00%)	1 / 28 (3.57%)	
occurrences (all)	0	1	
C-REACTIVE PROTEIN INCREASED			
subjects affected / exposed	3 / 33 (9.09%)	1 / 28 (3.57%)	
occurrences (all)	3	3	
ELECTROCARDIOGRAM QT			

PROLONGED			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences (all)	0	0	
WEIGHT DECREASED			
subjects affected / exposed	1 / 33 (3.03%)	2 / 28 (7.14%)	
occurrences (all)	1	2	
WEIGHT INCREASED			
subjects affected / exposed	1 / 33 (3.03%)	3 / 28 (10.71%)	
occurrences (all)	1	3	
Injury, poisoning and procedural complications			
CONTUSION			
subjects affected / exposed	1 / 33 (3.03%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
FALL			
subjects affected / exposed	1 / 33 (3.03%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
Cardiac disorders			
TACHYCARDIA			
subjects affected / exposed	1 / 33 (3.03%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			
HEADACHE			
subjects affected / exposed	5 / 33 (15.15%)	2 / 28 (7.14%)	
occurrences (all)	6	2	
DIZZINESS			
subjects affected / exposed	1 / 33 (3.03%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
DYSGEUSIA			
subjects affected / exposed	0 / 33 (0.00%)	1 / 28 (3.57%)	
occurrences (all)	0	1	
PERIPHERAL SENSORY NEUROPATHY			
subjects affected / exposed	1 / 33 (3.03%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
Blood and lymphatic system disorders			
ANAEMIA			

subjects affected / exposed	7 / 33 (21.21%)	7 / 28 (25.00%)	
occurrences (all)	13	7	
FEBRILE NEUTROPENIA			
subjects affected / exposed	2 / 33 (6.06%)	4 / 28 (14.29%)	
occurrences (all)	2	5	
LEUKOCYTOSIS			
subjects affected / exposed	3 / 33 (9.09%)	2 / 28 (7.14%)	
occurrences (all)	3	4	
LEUKOPENIA			
subjects affected / exposed	1 / 33 (3.03%)	1 / 28 (3.57%)	
occurrences (all)	6	3	
THROMBOCYTOPENIA			
subjects affected / exposed	5 / 33 (15.15%)	7 / 28 (25.00%)	
occurrences (all)	12	14	
NEUTROPENIA			
subjects affected / exposed	7 / 33 (21.21%)	4 / 28 (14.29%)	
occurrences (all)	10	7	
Eye disorders			
DRY EYE			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences (all)	0	0	
CONJUNCTIVAL HAEMORRHAGE			
subjects affected / exposed	2 / 33 (6.06%)	0 / 28 (0.00%)	
occurrences (all)	2	0	
Gastrointestinal disorders			
ABDOMINAL DISTENSION			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences (all)	0	0	
ABDOMINAL PAIN			
subjects affected / exposed	2 / 33 (6.06%)	1 / 28 (3.57%)	
occurrences (all)	2	1	
ABDOMINAL PAIN UPPER			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences (all)	0	0	
CONSTIPATION			

subjects affected / exposed	4 / 33 (12.12%)	6 / 28 (21.43%)	
occurrences (all)	4	6	
DIARRHOEA			
subjects affected / exposed	7 / 33 (21.21%)	6 / 28 (21.43%)	
occurrences (all)	7	6	
DRY MOUTH			
subjects affected / exposed	2 / 33 (6.06%)	0 / 28 (0.00%)	
occurrences (all)	2	0	
NAUSEA			
subjects affected / exposed	10 / 33 (30.30%)	7 / 28 (25.00%)	
occurrences (all)	18	8	
MOUTH HAEMORRHAGE			
subjects affected / exposed	1 / 33 (3.03%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
MELAENA			
subjects affected / exposed	2 / 33 (6.06%)	0 / 28 (0.00%)	
occurrences (all)	2	0	
HAEMORRHOIDS			
subjects affected / exposed	1 / 33 (3.03%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
GINGIVAL BLEEDING			
subjects affected / exposed	1 / 33 (3.03%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
DYSPEPSIA			
subjects affected / exposed	1 / 33 (3.03%)	1 / 28 (3.57%)	
occurrences (all)	1	1	
STOMATITIS			
subjects affected / exposed	7 / 33 (21.21%)	5 / 28 (17.86%)	
occurrences (all)	7	5	
VOMITING			
subjects affected / exposed	5 / 33 (15.15%)	1 / 28 (3.57%)	
occurrences (all)	5	2	
Hepatobiliary disorders			
HYPERBILIRUBINAEMIA			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences (all)	0	0	

Skin and subcutaneous tissue disorders			
ERYTHEMA			
subjects affected / exposed	1 / 33 (3.03%)	1 / 28 (3.57%)	
occurrences (all)	1	1	
RASH MACULO-PAPULAR			
subjects affected / exposed	1 / 33 (3.03%)	1 / 28 (3.57%)	
occurrences (all)	2	1	
RASH			
subjects affected / exposed	0 / 33 (0.00%)	1 / 28 (3.57%)	
occurrences (all)	0	1	
PRURITUS			
subjects affected / exposed	1 / 33 (3.03%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
PETECHIAE			
subjects affected / exposed	4 / 33 (12.12%)	0 / 28 (0.00%)	
occurrences (all)	5	0	
Renal and urinary disorders			
CHRONIC KIDNEY DISEASE			
subjects affected / exposed	1 / 33 (3.03%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
DYSURIA			
subjects affected / exposed	0 / 33 (0.00%)	1 / 28 (3.57%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
ARTHRALGIA			
subjects affected / exposed	0 / 33 (0.00%)	1 / 28 (3.57%)	
occurrences (all)	0	1	
BACK PAIN			
subjects affected / exposed	2 / 33 (6.06%)	1 / 28 (3.57%)	
occurrences (all)	2	1	
MUSCULAR WEAKNESS			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences (all)	0	0	
PAIN IN EXTREMITY			
subjects affected / exposed	5 / 33 (15.15%)	1 / 28 (3.57%)	
occurrences (all)	5	1	

Infections and infestations			
URINARY TRACT INFECTION			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences (all)	0	0	
BRONCHITIS			
subjects affected / exposed	2 / 33 (6.06%)	1 / 28 (3.57%)	
occurrences (all)	5	1	
CELLULITIS			
subjects affected / exposed	2 / 33 (6.06%)	1 / 28 (3.57%)	
occurrences (all)	2	1	
INFECTION			
subjects affected / exposed	0 / 33 (0.00%)	2 / 28 (7.14%)	
occurrences (all)	0	2	
ORAL CANDIDIASIS			
subjects affected / exposed	1 / 33 (3.03%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	0 / 33 (0.00%)	1 / 28 (3.57%)	
occurrences (all)	0	2	
TOOTH INFECTION			
subjects affected / exposed	2 / 33 (6.06%)	0 / 28 (0.00%)	
occurrences (all)	2	0	
RHINITIS			
subjects affected / exposed	0 / 33 (0.00%)	1 / 28 (3.57%)	
occurrences (all)	0	1	
PNEUMONIA FUNGAL			
subjects affected / exposed	0 / 33 (0.00%)	0 / 28 (0.00%)	
occurrences (all)	0	0	
PNEUMONIA			
subjects affected / exposed	0 / 33 (0.00%)	2 / 28 (7.14%)	
occurrences (all)	0	3	
PHARYNGITIS			
subjects affected / exposed	2 / 33 (6.06%)	0 / 28 (0.00%)	
occurrences (all)	2	0	
Metabolism and nutrition disorders			

DECREASED APPETITE			
subjects affected / exposed	5 / 33 (15.15%)	2 / 28 (7.14%)	
occurrences (all)	6	2	
HYPERGLYCAEMIA			
subjects affected / exposed	1 / 33 (3.03%)	2 / 28 (7.14%)	
occurrences (all)	1	2	
HYPERKALAEMIA			
subjects affected / exposed	0 / 33 (0.00%)	1 / 28 (3.57%)	
occurrences (all)	0	1	
HYPOCALCAEMIA			
subjects affected / exposed	0 / 33 (0.00%)	2 / 28 (7.14%)	
occurrences (all)	0	5	
HYPERURICAEMIA			
subjects affected / exposed	0 / 33 (0.00%)	1 / 28 (3.57%)	
occurrences (all)	0	1	
HYPOKALAEMIA			
subjects affected / exposed	2 / 33 (6.06%)	7 / 28 (25.00%)	
occurrences (all)	6	11	
HYPOMAGNESAEMIA			
subjects affected / exposed	2 / 33 (6.06%)	6 / 28 (21.43%)	
occurrences (all)	4	6	
HYPONATRAEMIA			
subjects affected / exposed	1 / 33 (3.03%)	1 / 28 (3.57%)	
occurrences (all)	1	3	
HYPOPHOSPHATAEMIA			
subjects affected / exposed	0 / 33 (0.00%)	1 / 28 (3.57%)	
occurrences (all)	0	1	
HYPOALBUMINAEMIA			
subjects affected / exposed	0 / 33 (0.00%)	2 / 28 (7.14%)	
occurrences (all)	0	3	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
30 November 2017	Sample size was increased and statistical considerations were updated. Study duration was updated. AG-221 background information was updated according to the current version of AG-221 (enasidenib) Investigator's Brochure (IB). The terminal half-life of enasidenib in humans was updated to 137 hours. Removal of evaluation of α-KG levels in plasma and bone marrow from exploratory endpoints Fasting (preferred) lipid panel was added at 2 more timepoints. The fasting requirement for lipid panel was updated. Frequency of assessing disease status in the follow-up phase was reduced. Data collection of investigator-assessed response/ disease status to subsequent AML therapies was added. Fasting requirement for taking AG-221 was removed. Reference toxicities during AG-221 therapy were updated. Restricted concomitant medications during AG-221 therapy were updated.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported