Clinical trial results:
A Phase 3, Multicenter, Randomized, Open-Label, Study of Azacitidine (Vidaza®) Versus Conventional Care Regimens for the Treatment of Older Subjects with Newly Diagnosed Acute Myeloid Leukemia

Summary

EudraCT number	2009-012346-23
Trial protocol	CZ DE BE FR GB ES NL AT IT
Global end of trial date	25 July 2016

Results information

Result version number	v1 (current)
This version publication date	10 August 2017
First version publication date	10 August 2017

Trial information

Trial identification

Sponsor protocol code	AZA-AML-001

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01074047
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Celgene Corporation
Sponsor organisation address	86 Morris Avenue, Summit, United States, 07901
Public contact	Clinical Trial Disclosure, Celgene Corporation, 01 888-260-1599, ClinicalTrialDisclosure@Celgene.com
Scientific contact	C.L. Beach Executive Medical Director, Celgene Corporation, 01 913-266-0302, CLBeach@celgene.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	28 February 2017
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	25 July 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study is to demonstrate superiority in overall survival (OS) of azacitidine compared with the combined conventional care regimens in subjects ≥ 65 years old who have newly diagnosed acute myeloid leukemia (AML) with > 30% bone marrow blasts.

Protection of trial subjects:

Patient Confidentiality, Personal Data Protection and Biomarker Consent

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	04 October 2010
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Regulatory reason
Long term follow-up duration	24 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Canada: 62
Country: Number of subjects enrolled	Poland: 62
Country: Number of subjects enrolled	Italy: 56
Country: Number of subjects enrolled	France: 45
Country: Number of subjects enrolled	Korea, Democratic People's Republic of: 47
Country: Number of subjects enrolled	Spain: 35
Country: Number of subjects enrolled	Germany: 32
Country: Number of subjects enrolled	United Kingdom: 26
Country: Number of subjects enrolled	Australia: 23
Country: Number of subjects enrolled	Belgium: 23
Country: Number of subjects enrolled	Russian Federation: 16
Country: Number of subjects enrolled	Taiwan: 15
Country: Number of subjects enrolled	Czech Republic: 12
Country: Number of subjects enrolled	Israel: 13
Country: Number of subjects enrolled	United States: 7
Country: Number of subjects enrolled	China: 6
Country: Number of subjects enrolled	Austria: 6
Country: Number of subjects enrolled	Netherlands: 2

Worldwide total number of subjects	488
EEA total number of subjects	299

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)	1
From 65 to 84 years	460
85 years and over	27

Subject disposition

Recruitment

Recruitment details:

This was a multicenter, international Phase 3 study conducted at 107 investigational sites in 18 countries including South Korea, China, Taiwan, Australia, Canada, United States, Poland, Russia, Czech Republic, Israel, France, Italy, Spain, Germany, United Kingdom, Belgium, Austria and the Netherlands.

Pre-assignment

Screening details:

Participants were randomized to either azacitidine or a conventional care regimen (CCR) assigned by the physician prior to randomization. Participants randomized to azacitidine and continuing to receive azacitidine at the time of study closure who did not meet any of the withdrawal criteria had the option of entering an extension phase.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Azacitidine (AZA)

Arm description:

Azacitidine 75 mg/m2/day by subcutaneous injection [SC] for 7 days every 28 days, with a 21-day rest period (optimally for at least 6 cycles) plus best supportive care as needed, including antibiotics and blood product transfusions, growth factors, per physician's discretion.

Arm type	Experimental
Investigational medicinal product name	Azacitidine
Investigational medicinal product code	L01BC07
Other name	Vidaza
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Azacitidine 75 mg/m2 every day (QD) by subcutaneous injection [SC] for 7 days every 28 days, with a 21-day rest period.

Arm title	Conventional Care Regimens (CCR)

Arm description:

#1 Intensive Chemotherapy: Cytarabine 100-200 mg/m² as a continuous intravenous infusion (CIVI) for 7 days and daunorubicin 45 to 60 mg/m² daily (QD) IV on Days 1, 2 and 3 or Idarubicin 9-12 mg/m² IV QD for 3 days. Consolidation Therapy (Cycle 2 and 3) = Cytarabine 100-200 mg/m² as a CIVI for 3 to 7 days and daunorubicin 45 to 60 mg/m² QD or Idarubicin 9-12 mg/m² IV QD on Days 1 and 2. Consolidation therapy started between Day 28 and Day 70 from start of induction therapy, upon recovery of absolute neutrophil count (ANC) above 1.0 x 10^9/L and platelets above 75 x 10^9/L. The second cycle started between Day 28 and Day 70 from start of first consolidation therapy. Best supportive care (BSC) of antibiotics and transfusions, were given as needed. # 2 Low-dose cytarabine 20 mg SC twice a day (BID) for 10 days every 28 days, plus BSC # 3 BSC only includes transfusion of blood products, antibiotics, antifungals and nutritional help.

Arm type	Active comparator
Investigational medicinal product name	Cytarabine
Investigational medicinal product code	
Other name	Cytosine arabinoside Tarabine PFS Ara-C Cytosar-U Depocyt
Pharmaceutical forms	Powder and solvent for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:	
Cytarabine 100-200 mg/m2 as a continuous intravenous infusion (CIVI) for 7 days during induction therapy followed by Cytarabine 100-200 mg/m2 as a CIVI for 3 to 7 days during consolidation therapy.	
Investigational medicinal product name	Daunorubicin
Investigational medicinal product code	
Other name	Cerubidine, Daunorubicin Hydrochloride for Injection, Daunoxome
Pharmaceutical forms	Powder and solvent for solution for infusion
Routes of administration	Intravenous use
Dosage and administration details:	
Daunorubicin 45 to 60 mg/m² QD by intravenous (IV) infusion on Days 1, 2 and 3 during induction therapy and QD on days 1 and 2 during consolidation therapy.	
Investigational medicinal product name	Idarubicin
Investigational medicinal product code	
Other name	Idamycin
Pharmaceutical forms	Powder and solvent for solution for infusion
Routes of administration	Intravenous use
Dosage and administration details:	
Idarubicin 9-12 mg/m² IV QD for 3 days	
Investigational medicinal product name	Low-dose Cytarabine
Investigational medicinal product code	
Other name	Cytarabine ARA-C Cytosar-U
Pharmaceutical forms	Powder and solvent for cutaneous solution
Routes of administration	Subcutaneous use
Dosage and administration details:	
Low-dose cytarabine 20 mg SC twice a day (BID) for 10 days every 28 days, plus BSC	
Investigational medicinal product name	Transfusion of blood products, antibiotics, antifungals and nutritional help
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard, Concentrate for solution for injection/infusion
Routes of administration	Intravenous use, Oral use
Dosage and administration details:	
Transfusion of blood products, antibiotics, antifungals and nutritional help as needed.	

Number of subjects in period 1	Azacitidine (AZA)	Conventional Care Regimens (CCR)
Started	241	247
Treated Population	236	240
Safety Population	236	235
Evaluable Population	179	191
Completed	24	13
Not completed	217	234
Adverse event, serious fatal	53	58
Consent withdrawn by subject	27	48
Adverse event, non-fatal	89	66
Miscellaneous	32	39
Lost to follow-up	-	1

Disease Progression	16	21
Protocol deviation	-	1

Period 2	
Period 2 title	Extension Phase
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Azacitidine (AZA)

Arm description:

Azacitidine 75 mg/m2/day by SC injection for 7 days every 28 days, with a 21 day rest period (optimally for at least 6 cycles) plus best supportive care as needed, including antibiotics and blood product transfusions, growth factors, per physician's discretion. Participants receiving AZA at the time the parent study was closed, were given the option to enter the extension phase at the same dose and schedule as long as they were not progressing or experienced toxicities.

Arm type	Experimental
Investigational medicinal product name	Azacitidine
Investigational medicinal product code	L01BC07
Other name	Vidaza
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Azacitidine 75 mg/m2 every day (QD) by subcutaneous injection [SC] for 7 days every 28 days, with a 21-day rest period.

Number of subjects in period 2[1]	Azacitidine (AZA)
Started	24
Safety Population	22
Completed	0
Not completed	24
Adverse event, serious fatal	5
Consent withdrawn by subject	2
Physician decision	1
Adverse event, non-fatal	5
Two subjects did not join extension phase	2
Disease Progression	9

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: Two patients elected not to participate in the extension phase and reason the number is less starting in the extension phase.

Baseline characteristics

Reporting groups	
Reporting group title	Azacitidine (AZA)
Reporting group description:	
Azacitidine 75 mg/m2/day by subcutaneous injection [SC] for 7 days every 28 days, with a 21-day rest period (optimally for at least 6 cycles) plus best supportive care as needed, including antibiotics and blood product transfusions, growth factors, per physician's discretion.	
Reporting group title	Conventional Care Regimens (CCR)
Reporting group description:	
#1 Intensive Chemotherapy: Cytarabine 100-200 mg/m² as a continuous intravenous infusion (CIVI) for 7 days and daunorubicin 45 to 60 mg/m² daily (QD) IV on Days 1, 2 and 3 or Idarubicin 9-12 mg/m² IV QD for 3 days. Consolidation Therapy (Cycle 2 and 3) = Cytarabine 100-200 mg/m² as a CIVI for 3 to 7 days and daunorubicin 45 to 60 mg/m² QD or Idarubicin 9-12 mg/m² IV QD on Days 1 and 2. Consolidation therapy started between Day 28 and Day 70 from start of induction therapy, upon recovery of absolute neutrophil count (ANC) above 1.0 x 10^9/L and platelets above 75 x 10^9/L. The second cycle started between Day 28 and Day 70 from start of first consolidation therapy. Best supportive care (BSC) of antibiotics and transfusions, were given as needed. # 2 Low-dose cytarabine 20 mg SC twice a day (BID) for 10 days every 28 days, plus BSC # 3 BSC only includes transfusion of blood products, antibiotics, antifungals and nutritional help.	

Reporting group values	Azacitidine (AZA)	Conventional Care Regimens (CCR)	Total
Number of subjects	241	247	488
Age Categorical Units: Subjects			
<75 years	103	120	223
≥75 years	138	127	265
Age Continuous Units: years			
arithmetic mean	75.4	75.1	
standard deviation	± 5.6	± 5.57	-
Gender, Male/Female Units: Subjects			
Female	102	98	200
Male	139	149	288
Eastern Cooperative Oncology Group (ECOG) Performance Status			
ECOG performance status is used by doctors and researchers to assess how a participant's disease is progressing, assess how the disease affects the daily living activities of the participant and determine appropriate treatment and prognosis. 0 = Fully Active (Most Favorable Activity), 1 = Restricted activity but ambulatory, 2 = Ambulatory but unable to carry out work activities, 3 = Limited Self Care; 4 = Completely Disabled, No self care (Least Favorable Activity)			
Units: Subjects			
0 = Fully Active	54	57	111
1 = Restrictive but Ambulatory	132	132	264
2 = Ambulatory but unable to work	55	58	113
3 = Limited Self-Care	0	0	0
4 = Completely disabled	0	0	0
World Health Organization Acute Myeloid Leukemia (AML) Classification			
WHO categories include: 1. Those with AML with recurrent genetic abnormalities. Includes subtypes with multiple chromosome translocations and mutations. 2. Those with AML with myelodysplasia-related changes. Includes those with prior myelodysplastic syndrome (MDS) or myeloproliferative disease and has transformed to AML. 3. Those with therapy related myeloid neoplasms and have had prior			

chemotherapy and/or radiation and subsequently develop AML or MDS 4. Those with AML not otherwise specified and include subtypes that do not fall into the above categories.			
Units: Subjects			
AML with myelodysplasia-related changes	75	83	158
Therapy-related myeloid neoplasms	8	12	20
AML with recurrent genetic abnormalities	5	9	14
AML not otherwise specified	153	143	296
Study Specific Characteristic | Bone Marrow Blasts			
Baseline clinical characteristics, including percentage of bone marrow blasts were assessed centrally and locally. Central values are included here. Baseline blasts were the last non-missing value on or prior to the date of randomization. The bone marrow blasts cells are not typically found in the circulating blood of healthy individuals. Abnormal immature white blood cells (blasts) fill the bone marrow and spill into the bloodstream.			
Units: Percentage of Bone Marrow Blasts			
arithmetic mean	66.6	70.2	
standard deviation	± 24.71	± 22.8	-

End points

End points reporting groups

Reporting group title	Azacitidine (AZA)

Reporting group description:

Azacitidine 75 mg/m2/day by subcutaneous injection [SC] for 7 days every 28 days, with a 21-day rest period (optimally for at least 6 cycles) plus best supportive care as needed, including antibiotics and blood product transfusions, growth factors, per physician's discretion.

Reporting group title	Conventional Care Regimens (CCR)

Reporting group description:

#1 Intensive Chemotherapy: Cytarabine 100-200 mg/m² as a continuous intravenous infusion (CIVI) for 7 days and daunorubicin 45 to 60 mg/m² daily (QD) IV on Days 1, 2 and 3 or Idarubicin 9-12 mg/m² IV QD for 3 days. Consolidation Therapy (Cycle 2 and 3) = Cytarabine 100-200 mg/m² as a CIVI for 3 to 7 days and daunorubicin 45 to 60 mg/m² QD or Idarubicin 9-12 mg/m² IV QD on Days 1 and 2. Consolidation therapy started between Day 28 and Day 70 from start of induction therapy, upon recovery of absolute neutrophil count (ANC) above 1.0 x 10^9/L and platelets above 75 x 10^9/L. The second cycle started between Day 28 and Day 70 from start of first consolidation therapy. Best supportive care (BSC) of antibiotics and transfusions, were given as needed. # 2 Low-dose cytarabine 20 mg SC twice a day (BID) for 10 days every 28 days, plus BSC # 3 BSC only includes transfusion of blood products, antibiotics, antifungals and nutritional help.

Reporting group title	Azacitidine (AZA)

Reporting group description:

Azacitidine 75 mg/m2/day by SC injection for 7 days every 28 days, with a 21 day rest period (optimally for at least 6 cycles) plus best supportive care as needed, including antibiotics and blood product transfusions, growth factors, per physician's discretion. Participants receiving AZA at the time the parent study was closed, were given the option to enter the extension phase at the same dose and schedule as long as they were not progressing or experienced toxicities.

Primary: Kaplan-Meier Estimates for Overall Survival

End point title	Kaplan-Meier Estimates for Overall Survival

End point description:

Overall Survival was defined as the time from randomization to death from any cause. Overall survival was calculated by the formula: date of death - date of randomization + 1. Participants surviving at the end of the follow-up period or who withdrew consent to follow-up were censored at the date of last contact. Participants who were lost to follow-up were censored at the date last known alive. ITT population defined as all subjects who were randomized, independent of whether they received study treatment or not. Includes participants who died and subjects who were censored.

End point type	Primary

End point timeframe:

Day 1 (randomization) to 40 months

End point values	Azacitidine (AZA)	Conventional Care Regimens (CCR)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	241	247		
Units: months				
median (confidence interval 95%)	10.4 (8 to 12.7)	6.5 (5 to 8.6)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

The hazard ratio is from a Cox proportional hazards model stratified by ECOG performance status and cytogenetic risk status.

Comparison groups	Azacitidine (AZA) v Conventional Care Regimens (CCR)
Number of subjects included in analysis	488
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1009 [1]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.85
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.69
upper limit	1.03

Notes:

[1] - The p-value is two-sided from a log-rank test stratified by ECOG performance status, and cytogenetic risk status.

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

The hazard ratio is from an unstratified Cox proportional hazards model.

Comparison groups	Azacitidine (AZA) v Conventional Care Regimens (CCR)
Number of subjects included in analysis	488
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0829 [2]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.84
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.69
upper limit	1.02

Notes:

[2] - The p-value is two-sided from a log-rank test stratified by ECOG performance status, and cytogenetic risk status.

Secondary: One-Year Overall Survival Rate

End point title	One-Year Overall Survival Rate

End point description:

Kaplan Meier methods were used to estimate the 1-year survival probabilities for time to death from any cause. ITT population defined as all subjects who were randomized, independent of whether they received study treatment or not. Includes those who died and subjects who were censored.

End point type	Secondary

End point timeframe:

From Day 1 (randomization) to 40 months

End point values	Azacitidine (AZA)	Conventional Care Regimens (CCR)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	241	247		
Units: percentage of participants				
number (confidence interval 95%)	46.5 (40.1 to 52.7)	34.3 (28.3 to 40.3)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Estimates of the 1-year (365 day) survival probabilities and corresponding 95% confidence intervals (CI) were presented by treatment group. The CI for the difference in the 1-year survival probabilities was derived using Greenwoods variance estimate.

Comparison groups	Azacitidine (AZA) v Conventional Care Regimens (CCR)
Number of subjects included in analysis	488
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Difference
Point estimate	12.26
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.5
upper limit	21

Secondary: Event-Free Survival (EFS)

End point title	Event-Free Survival (EFS)

End point description:

EFS was defined as the interval from the date of randomization to the date of treatment failure, progressive disease, relapse after complete remission (CR) or complete remission with incomplete blood count recovery (CRi), death from any cause, or lost to follow-up, whichever occurs first. Participants who were still alive without any of these events were censored at the date of their last response assessment. ITT population defined as all subjects who were randomized, independent of whether they received study treatment or not. Includes those who died and subjects who were censored.

End point type	Secondary

End point timeframe:

Day 1 (randomization) to date of treatment failure, progressive disease, relapse after Complete Remission (CR) or Complete remission with incomplete blood count recovery (CRi), death from any cause. Day 1 (randomization) to 40 months

End point values	Azacitidine (AZA)	Conventional Care Regimens (CCR)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	241	247		
Units: months				
median (confidence interval 95%)	6.7 (5 to 8.8)	4.8 (3.8 to 6)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

The hazard ratio is from an unstratified Cox proportional hazards model.

Comparison groups	Azacitidine (AZA) v Conventional Care Regimens (CCR)
Number of subjects included in analysis	488
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1495 [3]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.87
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.72
upper limit	1.05

Notes:

[3] - 2 sided unstratified

Secondary: Relapse-Free Survival (RFS) for Subjects who Achieved a Complete Remission (CR) or Complete remission with Incomplete Blood Count Recovery (CRi)

End point title	Relapse-Free Survival (RFS) for Subjects who Achieved a Complete Remission (CR) or Complete remission with Incomplete Blood Count Recovery (CRi)

End point description:

Relapse-free survival was defined as the interval from the date of first documented CR or CRi to the date of relapse, death from any cause, or lost to follow-up, whichever occurred first. Includes subjects who were still alive and in continuous CR or CRi were censored at the date of their last response assessment.

End point type	Secondary

End point timeframe:

Day 1 of first documented CR or CRi to the date of relapse, death from any cause, or lost to follow-up. Day 1 (randomization) to 40 months

End point values	Azacitidine (AZA)	Conventional Care Regimens (CCR)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	67	62		
Units: months				
median (confidence interval 95%)	9.3 (6.7 to 12.4)	10.5 (7.3 to 12.3)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

The hazard ratio is from an unstratified Cox proportional hazards model.

Comparison groups	Azacitidine (AZA) v Conventional Care Regimens (CCR)
Number of subjects included in analysis	129
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5832 [4]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.11
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.75
upper limit	1.66

Notes:

[4] - 2 sided unstratified

Secondary: Percentage of Subjects who Achieved a Morphologic CR + CRi as Determined by the Independent Review Committee (IRC) Based on International Working Group (IWG) Response Criteria for Acute Myeloid Leukemia (AML)

End point title	Percentage of Subjects who Achieved a Morphologic CR + CRi as Determined by the Independent Review Committee (IRC) Based on International Working Group (IWG) Response Criteria for Acute Myeloid Leukemia (AML)

End point description:

A complete remission (CR) is defined as a leukemia-free state defined as less than 5% blasts in a BM aspirate with marrow spicules and with at least 200 nucleated cells (there should be no blasts with Auer rods), an absolute neutrophil count (ANC) of ≥ 1 x 10^9/L, a platelet count ≥ 100 x 10^9/L, and transfusion independence (no transfusions for 1 week prior to each assessment). No duration of these findings is required for confirmation of this response. A CR with incomplete blood count recovery (CRi) is defined as <5% BM blasts with the ANC count < 1 x 10^9/L and/or the platelet count may be < 100 x 10^9/L. Where the date of the hematology assessment used is the earliest on or following the date of the BM sample up to 8 days after the BM date. ITT population.

End point type	Secondary

End point timeframe:

Day 1 (randomization) to 40 months

End point values	Azacitidine (AZA)	Conventional Care Regimens (CCR)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	241	247		
Units: percentage of subjects				
number (not applicable)	27.8	25.1		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Azacitidine (AZA) v Conventional Care Regimens (CCR)
Number of subjects included in analysis	488
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5384
Method	Fisher exact

Secondary: Duration of Remission Assessed by the IRC Based on Kaplan-Meier Estimates

End point title	Duration of Remission Assessed by the IRC Based on Kaplan-Meier Estimates

End point description:

The time from the date CR or CRi was first documented until the date of documented relapse from CR/CRi. Duration of remission was defined only for those subjects who achieved a CR or CRi, as determined by the IRC. Subjects who were lost to follow-up without documented relapse, or were alive at last follow-up without documented relapse were censored at the date of their last response assessment. Includes those with a CR or CRi.

End point type	Secondary

End point timeframe:

Day 1 (randomization) to 40 months; date of the first documented CR or CRi until date of first documented relapse.

End point values	Azacitidine (AZA)	Conventional Care Regimens (CCR)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	67	62		
Units: months				
median (confidence interval 95%)	10.4 (7.2 to 15.2)	12.3 (9 to 17)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects who Achieved a Cytogenetic Complete Remission (CRc-10) as Determined by the IRC

End point title	Number of Subjects who Achieved a Cytogenetic Complete Remission (CRc-10) as Determined by the IRC

End point description:

The CRc is a normal karyotype defined as no clonal abnormalities after review of at least 10 metaphases using conventional cytogenetic techniques. Cytogenetic complete remission rate (CRc) is based on the following criteria: 1) CR criteria met and 2) an abnormal karyotype is present at baseline and 3) there is reversion to normal karyotype at the time of CR (based on ≥ 10 metaphases), where date of cytogenetic sample = date of BM sample used for the CR assessment. ITT population defined as all subjects who were randomized, independent of whether they received study treatment or not. Includes subjects who died and participants who were censored.

End point type	Secondary

End point timeframe:

Day 1 (randomization) to 40 months

End point values	Azacitidine (AZA)	Conventional Care Regimens (CCR)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	241	247		
Units: participants	5	15		

Statistical analyses

Statistical analysis title	Statistical Analysis
Comparison groups	Azacitidine (AZA) v Conventional Care Regimens (CCR)
Number of subjects included in analysis	488
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0376
Method	Fisher exact

Secondary: Number of Subjects with Adverse Events (AEs).

End point title	Number of Subjects with Adverse Events (AEs).

End point description:

AEs = any noxious, unintended, or untoward medical occurrence that may appear or worsen during the course of a study. It may be a new intercurrent illness, a worsening concomitant illness, an injury, or any concomitant impairment of the participant's health, regardless of cause. Serious AE (SAE) = any AE which 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; constitutes an important medical event. The severity of AEs were graded based upon the participants symptoms according to the Common Terminology Criteria for Adverse Events (CTCAE, Version 4.0); AEs were evaluated for severity according to the following scale: Grade 1 = Mild – transient or mild discomfort; no medical intervention required; Grade 2 = Moderate – mild to moderate limitation in activity; Grade 3 = Severe; Grade 4 = Life threatening; Grade 5 = Death.

End point type	Secondary

End point timeframe:

Day 1 (randomization) up to last visit completed 22 Jan 2014; Up to 40 months

End point values	Azacitidine (AZA)	Conventional Care Regimens (CCR)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	236	235		
Units: subjects				
At least one Treatment Emergent AE	234	231		
At least one TEAE related to study drug	188	163		
Grade 3-4 adverse event	207	204		
Grade 3-4 adverse event related to any study drug	125	119		
At least one Grade 5 (leading to death) TEAE	56	70		
Grade 5 adverse event related to any study drug	12	14		
Serious TEAE	188	175		
Serious TEAE related to any study drug	87	70		
TEAE leading to discontinuation of study drug	110	79		
Study drug-related TEAE leading to discontinuation	22	25		
TEAE leading to study drug dose reduction	8	4		
TEAE leading to study drug dose interruption	116	65		
TEAE causing study drug dose reduction/disruption	13	7		

Statistical analyses

No statistical analyses for this end point

Secondary: Health Related Quality of Life (HRQoL): Change from Baseline in the European Organization for Research and Treatment of Cancer Cancer Quality of Life Questionnaire for Patients with Cancer (EORTC QLQ-C30) Fatigue Domain

End point title	Health Related Quality of Life (HRQoL): Change from Baseline in the European Organization for Research and Treatment of Cancer Cancer Quality of Life Questionnaire for Patients with

	Cancer (EORTC QLQ-C30) Fatigue Domain

End point description:

The European Organization for Research and Treatment of Cancer (EORTC) Core Quality of Life (QOL) questionnaire (EORTC QLQ-C30) is a 30-question tool used to assess the overall QOL in cancer patients. It consists of 15 domains: 1 global health status (GHS) scale, 5 functional scales (Physical, Role, Cognitive, Emotional, Social), and 9 symptom scales/items (Fatigue, Nausea and Vomiting, Pain, Dyspnea, Sleep Disturbance, Appetite Loss, Constipation, Diarrhea, Financial Impact). The EORTC QLQ-C30 Fatigue Scale is scored between 0 and 100, with a high score indicating a higher level of symptoms. Negative change from Baseline values indicate reduction in fatigue (i.e. improvement in symptom) and positive values indicate increases in fatigue (i.e. worsening of symptom). The HRQoL Evaluable population included only participants with a baseline QoL assessment and at least 1 follow-up assessment. Time windows were applied post-hoc to increase the size of the analyzable population.

End point type	Secondary

End point timeframe:

Baseline to Cycle 3; at approximately 3 months

End point values	Azacitidine (AZA)	Conventional Care Regimens (CCR)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	135	101		
Units: units on a scale				
arithmetic mean (standard deviation)	-1.5 (± 24.69)	-1.9 (± 27.54)		

Statistical analyses

No statistical analyses for this end point

Secondary: Health Related Quality of Life (HRQoL): Change from Baseline in the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire for Patients with Cancer (EORTC QLQ-C30) Fatigue Domain

End point title	Health Related Quality of Life (HRQoL): Change from Baseline in the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire for Patients with Cancer (EORTC QLQ-C30) Fatigue Domain

End point description:

The European Organization for Research and Treatment of Cancer (EORTC) Core Quality of Life (QOL) questionnaire (EORTC QLQ-C30) is a 30-question tool used to assess the overall QOL in cancer patients. It consists of 15 domains: 1 global health status (GHS) scale, 5 functional scales (Physical, Role, Cognitive, Emotional, Social), and 9 symptom scales/items (Fatigue, Nausea and Vomiting, Pain, Dyspnea, Sleep Disturbance, Appetite Loss, Constipation, Diarrhea, Financial Impact). The EORTC QLQ-C30 Fatigue Scale is scored between 0 and 100, with a high score indicating a higher level of symptoms. Negative change from Baseline values indicate reduction in fatigue (i.e. improvement in symptom) and positive values indicate increases in fatigue (i.e. worsening of symptom). The HRQoL Evaluable population included only participants with a baseline QoL assessment and at least 1 follow-up assessment. Time windows were applied post-hoc to increase the size of the analyzable population.

End point type	Secondary

End point timeframe:

Baseline to Cycle 5, at approximately 5 months

End point values	Azacitidine (AZA)	Conventional Care Regimens (CCR)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	112	66		
Units: units on a scale				
arithmetic mean (standard deviation)	-2.8 (± 27.36)	-7.1 (± 27.61)		

Statistical analyses

No statistical analyses for this end point

Secondary: Health Related Quality of Life (HRQoL): Change from Baseline in the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire for Patients with Cancer (EORTC QLQ-C30) Fatigue Domain

End point title	Health Related Quality of Life (HRQoL): Change from Baseline in the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire for Patients with Cancer (EORTC QLQ-C30) Fatigue Domain

End point description:

The European Organization for Research and Treatment of Cancer (EORTC) Core Quality of Life (QOL) questionnaire (EORTC QLQ-C30) is a 30-question tool used to assess the overall QOL in cancer patients. It consists of 15 domains: 1 global health status (GHS) scale, 5 functional scales (Physical, Role, Cognitive, Emotional, Social), and 9 symptom scales/items (Fatigue, Nausea and Vomiting, Pain, Dyspnea, Sleep Disturbance, Appetite Loss, Constipation, Diarrhea, Financial Impact). The EORTC QLQ-C30 Fatigue Scale is scored between 0 and 100, with a high score indicating a higher level of symptoms. Negative change from Baseline values indicate reduction in fatigue (i.e. improvement in symptom) and positive values indicate increases in fatigue (i.e. worsening of symptom). The HRQoL Evaluable population included only participants with a baseline QoL assessment and at least 1 follow-up assessment. Time windows were applied post-hoc to increase the size of the analyzable population.

End point type	Secondary

End point timeframe:

Baseline to Cycle 7, at approximately 7 months

End point values	Azacitidine (AZA)	Conventional Care Regimens (CCR)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	94	53		
Units: units on a scale				
arithmetic mean (standard deviation)	-6.1 (± 26.9)	-12.2 (± 30.45)		

Statistical analyses

No statistical analyses for this end point

Secondary: Health Related Quality of Life (HRQoL): Change from Baseline in the European Organization for Research and Treatment of Cancer Quality of Life

Questionnaire for Patients with Cancer (EORTC QLQ-C30) Fatigue Domain

End point title	Health Related Quality of Life (HRQoL): Change from Baseline in the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire for Patients with Cancer (EORTC QLQ-C30) Fatigue Domain

End point description:

The European Organization for Research and Treatment of Cancer (EORTC) Core Quality of Life (QOL) questionnaire (EORTC QLQ-C30) is a 30-question tool used to assess the overall QOL in cancer patients. It consists of 15 domains: 1 global health status (GHS) scale, 5 functional scales (Physical, Role, Cognitive, Emotional, Social), and 9 symptom scales/items (Fatigue, Nausea and Vomiting, Pain, Dyspnea, Sleep Disturbance, Appetite Loss, Constipation, Diarrhea, Financial Impact). The EORTC QLQ-C30 Fatigue Scale is scored between 0 and 100, with a high score indicating a higher level of symptoms. Negative change from Baseline values indicate reduction in fatigue (i.e. improvement in symptom) and positive values indicate increases in fatigue (i.e. worsening of symptom). The HRQoL Evaluable population included only participants with a baseline QoL assessment and at least 1 follow-up assessment. Time windows were applied post-hoc to increase the size of the analyzable population.

End point type	Secondary

End point timeframe:

Baseline to Cycle 9, at approximately 9 months

End point values	Azacitidine (AZA)	Conventional Care Regimens (CCR)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	80	36		
Units: units on a scale				
arithmetic mean (standard deviation)	-9 (± 27.9)	-10.2 (± 33.85)		

Statistical analyses

No statistical analyses for this end point

Secondary: Health Related Quality of Life (HRQoL): Change from Baseline in the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire for Patients with Cancer (EORTC QLQ-C30) Fatigue Domain

End point title	Health Related Quality of Life (HRQoL): Change from Baseline in the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire for Patients with Cancer (EORTC QLQ-C30) Fatigue Domain

End point description:

The European Organization for Research and Treatment of Cancer (EORTC) Core Quality of Life (QOL) questionnaire (EORTC QLQ-C30) is a 30-question tool used to assess the overall QOL in cancer patients. It consists of 15 domains: 1 global health status (GHS) scale, 5 functional scales (Physical, Role, Cognitive, Emotional, Social), and 9 symptom scales/items (Fatigue, Nausea and Vomiting, Pain, Dyspnea, Sleep Disturbance, Appetite Loss, Constipation, Diarrhea, Financial Impact). The EORTC QLQ-C30 Fatigue Scale is scored between 0 and 100, with a high score indicating a higher level of symptoms. Negative change from Baseline values indicate reduction in fatigue (i.e. improvement in symptom) and positive values indicate increases in fatigue (i.e. worsening of symptom). The HRQoL Evaluable population included only participants with a baseline QoL assessment and at least 1 follow-up assessment. Time windows were applied post-hoc to increase the size of the analyzable population.

End point type	Secondary

End point timeframe:

Baseline to End of Study; at approximately 11-12 months

End point values	Azacitidine (AZA)	Conventional Care Regimens (CCR)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	87	80		
Units: units on a scale				
arithmetic mean (standard deviation)	8.9 (± 33.54)	6.1 (± 34.19)		

Statistical analyses

No statistical analyses for this end point

Secondary: HRQoL: Change from Baseline in the EORTC QLQ-C30 Dyspnea

End point title	HRQoL: Change from Baseline in the EORTC QLQ-C30 Dyspnea

End point description:

The European Organization for Research and Treatment of Cancer (EORTC) Core Quality of Life (QOL) questionnaire (EORTC QLQ-C30) is a 30-question tool used to assess the overall QOL in cancer patients. It consists of 15 domains: 1 global health status (GHS) scale, 5 functional scales (Physical, Role, Cognitive, Emotional, Social), and 9 symptom scales/items (Fatigue, Nausea and Vomiting, Pain, Dyspnea, Sleep Disturbance, Appetite Loss, Constipation, Diarrhea, Financial Impact). The EORTC QLQ-C30 Dyspnea scale is scored between 0 and 100, with a high score indicating a higher level of symptoms. Negative change from Baseline values indicate decreased dyspnea (i.e. improvement in symptom) and positive values indicate increased dyspnea (i.e. worsening of symptom). The HRQoL Evaluable population included only participants with a baseline QoL assessment and at least 1 follow-up assessment. Time windows were applied post-hoc to increase the size of the analyzable population.

End point type	Secondary

End point timeframe:

Baseline to Cycle 3, at approximately 3 months

End point values	Azacitidine (AZA)	Conventional Care Regimens (CCR)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	136	101		
Units: units on a scale				
arithmetic mean (standard deviation)	5.1 (± 26.88)	-1.7 (± 30.69)		

Statistical analyses

No statistical analyses for this end point

Secondary: HRQoL: Change from Baseline in the EORTC QLQ-C30 Dyspnea

End point title	HRQoL: Change from Baseline in the EORTC QLQ-C30 Dyspnea

End point description:

The European Organization for Research and Treatment of Cancer (EORTC) Core Quality of Life (QOL) questionnaire (EORTC QLQ-C30) is a 30-question tool used to assess the overall QOL in cancer patients. It consists of 15 domains: 1 global health status (GHS) scale, 5 functional scales (Physical, Role, Cognitive, Emotional, Social), and 9 symptom scales/items (Fatigue, Nausea and Vomiting, Pain, Dyspnea, Sleep Disturbance, Appetite Loss, Constipation, Diarrhea, Financial Impact). The EORTC QLQ-C30 Dyspnea scale is scored between 0 and 100, with a high score indicating a higher level of symptoms. Negative change from Baseline values indicate decreased dyspnea (i.e. improvement in symptom) and positive values indicate increased dyspnea (i.e. worsening of symptom). The HRQoL Evaluable population included only participants with a baseline QoL assessment and at least 1 follow-up assessment. Time windows were applied post-hoc to increase the size of the analyzable population.

End point type	Secondary

End point timeframe:

Baseline to Cycle 5, at approximately 5 months

End point values	Azacitidine (AZA)	Conventional Care Regimens (CCR)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	112	66		
Units: units on a scale				
arithmetic mean (standard deviation)	3.9 (± 27.49)	-6.6 (± 28.18)		

Statistical analyses

No statistical analyses for this end point

Secondary: HRQoL: Change from Baseline in the EORTC QLQ-C30 Dyspnea

End point title	HRQoL: Change from Baseline in the EORTC QLQ-C30 Dyspnea

End point description:

The European Organization for Research and Treatment of Cancer (EORTC) Core Quality of Life (QOL) questionnaire (EORTC QLQ-C30) is a 30-question tool used to assess the overall QOLin cancer patients. It consists of 15 domains: 1 global health status (GHS) scale, 5 functional scales (Physical, Role, Cognitive, Emotional, Social), and 9 symptom scales/items (Fatigue, Nausea and Vomiting, Pain, Dyspnea, Sleep Disturbance, Appetite Loss, Constipation, Diarrhea, Financial Impact). The EORTC QLQ-C30 Dyspnea scale is scored between 0 and 100, with a high score indicating a higher level of symptoms. Negative change from Baseline values indicate decreased dyspnea (i.e. improvement in symptom) and positive values indicate increased dyspnea (i.e. worsening of symptom). The HRQoL Evaluable population included only participants with a baseline QoL assessment and at least 1 follow-up assessment. Time windows were applied post-hoc to increase the size of the analyzable population.

End point type	Secondary

End point timeframe:

Baseline to Cycle 7, at approximately 7 months

End point values	Azacitidine (AZA)	Conventional Care Regimens (CCR)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	94	53		
Units: units on a scale				
arithmetic mean (standard deviation)	0.4 (± 29.93)	-8.8 (± 28.61)		

Statistical analyses

No statistical analyses for this end point

Secondary: HRQoL: Change from Baseline in the EORTC QLQ-C30 Dyspnea

End point title	HRQoL: Change from Baseline in the EORTC QLQ-C30 Dyspnea

End point description:

The EORTC Core Quality of Life (QOL) questionnaire (EORTC QLQ-C30) is a 30-question tool used to assess the overall QOL in cancer patients. It consists of 15 domains: 1 global health status (GHS) scale, 5 functional scales (Physical, Role, Cognitive, Emotional, Social), and 9 symptom scales/items (Fatigue, Nausea and Vomiting, Pain, Dyspnea, Sleep Disturbance, Appetite Loss, Constipation, Diarrhea, Financial Impact). The dyspnea scale is scored between 0 and 100, with a high score indicating a higher level of symptoms. Negative change from baseline values indicate decreased dyspnea and positive values indicate increased dyspnea. The HRQoL Evaluable population included only yhose with a baseline QoL assessment and at least 1 follow-up assessment. Time windows were applied post-hoc to increase the size of the analyzable population. The analysis included 157 from the azacitidine group and 134 in the CCR group, a smaller number than the ITT population.

End point type	Secondary

End point timeframe:

Baseline to Cycle 9, at approximately 9 months

End point values	Azacitidine (AZA)	Conventional Care Regimens (CCR)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	81	36		
Units: units on a scale				
arithmetic mean (standard deviation)	-4.9 (± 26.93)	-2.8 (± 26.87)		

Statistical analyses

No statistical analyses for this end point

Secondary: HRQoL: Change from Baseline in the EORTC QLQ-C30 Dyspnea

End point title	HRQoL: Change from Baseline in the EORTC QLQ-C30 Dyspnea

End point description:

The European Organization for Research and Treatment of Cancer (EORTC) Core Quality of Life (QOL) questionnaire (EORTC QLQ-C30) is a 30-question tool used to assess the overall QOL in cancer patients. It consists of 15 domains: 1 global health status (GHS) scale, 5 functional scales (Physical, Role, Cognitive, Emotional, Social), and 9 symptom scales/items (Fatigue, Nausea and Vomiting, Pain,

Dyspnea, Sleep Disturbance, Appetite Loss, Constipation, Diarrhea, Financial Impact). The EORTC QLQ-C30 Physical Functioning scale is scored between 0 and 100, with a high score indicating a higher level of symptoms. Negative change from Baseline values indicate decreased dyspnea (i.e. improvement in symptom) and positive values indicate increased dyspnea (i.e. worsening of symptom). The HRQoL Evaluable population included only participants with a baseline QoL assessment and at least 1 follow-up assessment. Time windows were applied post-hoc to increase the size of the analyzable population.

End point type	Secondary

End point timeframe:

Baseline to end of study, at approximately 11-12 months

End point values	Azacitidine (AZA)	Conventional Care Regimens (CCR)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	87	80		
Units: units on a scale				
arithmetic mean (standard deviation)	12.6 (± 31.43)	6.3 (± 35.22)		

Statistical analyses

Statistical analysis title	Statistical Analysis 2
Comparison groups	Azacitidine (AZA) v Conventional Care Regimens (CCR)
Number of subjects included in analysis	167
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1164 [5]
Method	t-test, 2-sided

Notes:

[5] - p-value for CCR is calculated using the paired t-test on the observed domain score, comparing with baseline.

Secondary: HRQoL: Change from Baseline in the EORTC QLQ-C30 Physical Functioning Domain

End point title	HRQoL: Change from Baseline in the EORTC QLQ-C30 Physical Functioning Domain

End point description:

The European Organization for Research and Treatment of Cancer (EORTC) Core Quality of Life (QOL) questionnaire (EORTC QLQ-C30) is a 30-question tool used to assess the overall QOL in cancer patients. It consists of 15 domains: 1 global health status (GHS) scale, 5 functional scales (Physical, Role, Cognitive, Emotional, Social), and 9 symptom scales/items (Fatigue, Nausea and Vomiting, Pain, Dyspnea, Sleep Disturbance, Appetite Loss, Constipation, Diarrhea, Financial Impact). The EORTC QLQ-C30 Physical Functioning Scale is scored between 0 and 100, with a high score indicating better functioning. Negative change from Baseline values indicate deterioration in functioning and positive values indicate improvement. The HRQoL Evaluable population included only participants with a baseline QoL assessment and at least 1 follow-up assessment. Time windows were applied post-hoc to increase the size of the analyzable population.

End point type	Secondary

End point timeframe:

Baseline to Cycle 3, at approximately 3 months

End point values	Azacitidine (AZA)	Conventional Care Regimens (CCR)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	136	102		
Units: units on a scale				
arithmetic mean (standard deviation)	-4.2 (± 17.98)	-0.3 (± 18.85)		

Statistical analyses

No statistical analyses for this end point

Secondary: HRQoL: Change from Baseline in the EORTC QLQ-C30 Physical Functioning Domain

End point title	HRQoL: Change from Baseline in the EORTC QLQ-C30 Physical Functioning Domain

End point description:

The European Organization for Research and Treatment of Cancer (EORTC) Core Quality of Life (QOL) questionnaire (EORTC QLQ-C30) is a 30-question tool used to assess the overall QOL in cancer patients. It consists of 15 domains: 1 global health status (GHS) scale, 5 functional scales (Physical, Role, Cognitive, Emotional, Social), and 9 symptom scales/items (Fatigue, Nausea and Vomiting, Pain, Dyspnea, Sleep Disturbance, Appetite Loss, Constipation, Diarrhea, Financial Impact). The EORTC QLQ-C30 Physical Functioning Scale is scored between 0 and 100, with a high score indicating better functioning. Negative change from Baseline values indicate deterioration in functioning and positive values indicate improvement. The HRQoL Evaluable population included only participants with a baseline QoL assessment and at least 1 follow-up assessment. Time windows were applied post-hoc to increase the size of the analyzable population.

End point type	Secondary

End point timeframe:

Baseline to Cycle 5, at approximately 5 months

End point values	Azacitidine (AZA)	Conventional Care Regimens (CCR)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	112	67		
Units: units on a scale				
arithmetic mean (standard deviation)	-4.4 (± 19.25)	-1.3 (± 20.41)		

Statistical analyses

No statistical analyses for this end point

Secondary: HRQoL: Change from Baseline in the EORTC QLQ-C30 Physical

Functioning Domain

End point title	HRQoL: Change from Baseline in the EORTC QLQ-C30 Physical Functioning Domain

End point description:

The European Organization for Research and Treatment of Cancer (EORTC) Core Quality of Life (QOL) questionnaire (EORTC QLQ-C30) is a 30-question tool used to assess the overall QOL in cancer patients. It consists of 15 domains: 1 global health status (GHS) scale, 5 functional scales (Physical, Role, Cognitive, Emotional, Social), and 9 symptom scales/items (Fatigue, Nausea and Vomiting, Pain, Dyspnea, Sleep Disturbance, Appetite Loss, Constipation, Diarrhea, Financial Impact). The EORTC QLQ-C30 Physical Functioning Scale is scored between 0 and 100, with a high score indicating better functioning. Negative change from Baseline values indicate deterioration in functioning and positive values indicate improvement. The HRQoL Evaluable population included only participants with a baseline QoL assessment and at least 1 follow-up assessment. Time windows were applied post-hoc to increase the size of the analyzable population.

End point type	Secondary

End point timeframe:

Baseline to Cycle 7, at approximately 7 months

End point values	Azacitidine (AZA)	Conventional Care Regimens (CCR)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	94	54		
Units: units on a scale				
arithmetic mean (standard deviation)	1.6 (± 18.75)	1.5 (± 23.08)		

Statistical analyses

No statistical analyses for this end point

Secondary: HRQoL: Change from Baseline in the EORTC QLQ-C30 Physical Functioning Domain

End point title	HRQoL: Change from Baseline in the EORTC QLQ-C30 Physical Functioning Domain

End point description:

The European Organization for Research and Treatment of Cancer (EORTC) Core Quality of Life (QOL) questionnaire (EORTC QLQ-C30) is a 30-question tool used to assess the overall QOL in cancer patients. It consists of 15 domains: 1 global health status (GHS) scale, 5 functional scales (Physical, Role, Cognitive, Emotional, Social), and 9 symptom scales/items (Fatigue, Nausea and Vomiting, Pain, Dyspnea, Sleep Disturbance, Appetite Loss, Constipation, Diarrhea, Financial Impact). The EORTC QLQ-C30 Physical Functioning Scale is scored between 0 and 100, with a high score indicating better functioning. Negative change from Baseline values indicate deterioration in functioning and positive values indicate improvement. The HRQoL Evaluable population included only participants with a baseline QoL assessment and at least 1 follow-up assessment. Time windows were applied post-hoc to increase the size of the analyzable population.

End point type	Secondary

End point timeframe:

Baseline to Cycle 9, at approximately 9 months

End point values	Azacitidine (AZA)	Conventional Care Regimens (CCR)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	81	36		
Units: units on a scale				
arithmetic mean (standard deviation)	3.5 (± 18.26)	-0.4 (± 22.81)		

Statistical analyses

No statistical analyses for this end point

Secondary: HRQoL: Change from Baseline in the EORTC QLQ-C30 Physical Functioning Domain

End point title	HRQoL: Change from Baseline in the EORTC QLQ-C30 Physical Functioning Domain

End point description:

The European Organization for Research and Treatment of Cancer (EORTC) Core Quality of Life (QOL) questionnaire (EORTC QLQ-C30) is a 30-question tool used to assess the overall QOL in cancer patients. It consists of 15 domains: 1 global health status (GHS) scale, 5 functional scales (Physical, Role, Cognitive, Emotional, Social), and 9 symptom scales/items (Fatigue, Nausea and Vomiting, Pain, Dyspnea, Sleep Disturbance, Appetite Loss, Constipation, Diarrhea, Financial Impact). The EORTC QLQ-C30 Physical Functioning Scale is scored between 0 and 100, with a high score indicating better functioning. Negative change from Baseline values indicate deterioration in functioning and positive values indicate improvement. The HRQoL Evaluable population included only participants with a baseline QoL assessment and at least 1 follow-up assessment. Time windows were applied post-hoc to increase the size of the analyzable population.

End point type	Secondary

End point timeframe:

Baseline to end of study, at approximately 11-12 months

End point values	Azacitidine (AZA)	Conventional Care Regimens (CCR)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	87	81		
Units: units on a scale				
arithmetic mean (standard deviation)	-13 (± 26.74)	-9.4 (± 26.43)		

Statistical analyses

No statistical analyses for this end point

Secondary: HRQoL: Change from Baseline in the EORTC QLQ-C30 Global Health Status-/Quality of Life Domain

End point title	HRQoL: Change from Baseline in the EORTC QLQ-C30 Global Health Status-/Quality of Life Domain

End point description:

The European Organization for Research and Treatment of Cancer (EORTC) Core Quality of Life (QOL) questionnaire (EORTC QLQ-C30) is a 30-question tool used to assess the overall QOL in cancer patients. It consists of 15 domains: 1 global health status (GHS) scale, 5 functional scales (Physical, Role, Cognitive, Emotional, Social), and 9 symptom scales/items (Fatigue, Nausea and Vomiting, Pain, Dyspnea, Sleep Disturbance, Appetite Loss, Constipation, Diarrhea, Financial Impact). The EORTC QLQ-C30 Global Health Status/QOL scale is scored between 0 and 100, with a high score indicating better Global Health Status/QOL. Negative change from Baseline values indicate deterioration in Global Health Status/QOL and positive values indicate improvement. The HRQoL Evaluable population included only participants with a baseline QoL assessment and at least 1 follow-up assessment. Time windows were applied post-hoc to increase the size of the analyzable population.

End point type	Secondary

End point timeframe:

Baseline to Cycle 3, at approximately 3 months

End point values	Azacitidine (AZA)	Conventional Care Regimens (CCR)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	134	101		
Units: units on a scale				
arithmetic mean (standard deviation)	0.9 (± 20.97)	3.8 (± 26.42)		

Statistical analyses

No statistical analyses for this end point

Secondary: HRQoL: Change from Baseline in the EORTC QLQ-C30 Global Health Status-/Quality of Life Domain

End point title	HRQoL: Change from Baseline in the EORTC QLQ-C30 Global Health Status-/Quality of Life Domain

End point description:

The European Organization for Research and Treatment of Cancer (EORTC) Core Quality of Life (QOL) questionnaire (EORTC QLQ-C30) is a 30-question tool used to assess the overall QOL in cancer patients. It consists of 15 domains: 1 global health status (GHS) scale, 5 functional scales (Physical, Role, Cognitive, Emotional, Social), and 9 symptom scales/items (Fatigue, Nausea and Vomiting, Pain, Dyspnea, Sleep Disturbance, Appetite Loss, Constipation, Diarrhea, Financial Impact). The EORTC QLQ-C30 Global Health Status/QOL scale is scored between 0 and 100, with a high score indicating better Global Health Status/QOL. Negative change from Baseline values indicate deterioration in Global Health Status/QOL and positive values indicate improvement. The HRQoL Evaluable population included only participants with a baseline QoL assessment and at least 1 follow-up assessment. Time windows were applied post-hoc to increase the size of the analyzable population.

End point type	Secondary

End point timeframe:

Baseline to Cycle 5, at approximately 5 months

End point values	Azacitidine (AZA)	Conventional Care Regimens (CCR)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	112	66		
Units: units on a scale				
arithmetic mean (standard deviation)	1.6 (± 22.5)	9 (± 24.82)		

Statistical analyses

No statistical analyses for this end point

Secondary: HRQoL: Change from Baseline in the EORTC QLQ-C30 Global Health Status-/Quality of Life Domain

End point title	HRQoL: Change from Baseline in the EORTC QLQ-C30 Global Health Status-/Quality of Life Domain

End point description:

The European Organization for Research and Treatment of Cancer (EORTC) Core Quality of Life (QOL) questionnaire (EORTC QLQ-C30) is a 30-question tool used to assess the overall QOL in cancer patients. It consists of 15 domains: 1 global health status (GHS) scale, 5 functional scales (Physical, Role, Cognitive, Emotional, Social), and 9 symptom scales/items (Fatigue, Nausea and Vomiting, Pain, Dyspnea, Sleep Disturbance, Appetite Loss, Constipation, Diarrhea, Financial Impact). The EORTC QLQ-C30 Global Health Status/QOL scale is scored between 0 and 100, with a high score indicating better Global Health Status/QOL. Negative change from Baseline values indicate deterioration in Global Health Status/QOL and positive values indicate improvement. The HRQoL Evaluable population included only participants with a baseline QoL assessment and at least 1 follow-up assessment. Time windows were applied post-hoc to increase the size of the analyzable population.

End point type	Secondary

End point timeframe:

Baseline to Cycle 7, at approximately 7 months

End point values	Azacitidine (AZA)	Conventional Care Regimens (CCR)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	94	52		
Units: units on a scale				
arithmetic mean (standard deviation)	5.1 (± 25.84)	8.7 (± 27.91)		

Statistical analyses

No statistical analyses for this end point

Secondary: HRQoL: Change from Baseline in the EORTC QLQ-C30 Global Health Status-/Quality of Life Domain

End point title	HRQoL: Change from Baseline in the EORTC QLQ-C30 Global Health Status-/Quality of Life Domain

End point description:

The European Organization for Research and Treatment of Cancer (EORTC) Core Quality of Life (QOL) questionnaire (EORTC QLQ-C30) is a 30-question tool used to assess the overall QOL in cancer patients. It consists of 15 domains: 1 global health status (GHS) scale, 5 functional scales (Physical, Role, Cognitive, Emotional, Social), and 9 symptom scales/items (Fatigue, Nausea and Vomiting, Pain, Dyspnea, Sleep Disturbance, Appetite Loss, Constipation, Diarrhea, Financial Impact). The EORTC QLQ-C30 Global Health Status/QOL scale is scored between 0 and 100, with a high score indicating better Global Health Status/QOL. Negative change from Baseline values indicate deterioration in Global Health Status/QOL and positive values indicate improvement. The HRQoL Evaluable population included only participants with a baseline QoL assessment and at least 1 follow-up assessment. Time windows were applied post-hoc to increase the size of the analyzable population.

End point type	Secondary

End point timeframe:

Baseline to Cycle 9, at approximately 9 months

End point values	Azacitidine (AZA)	Conventional Care Regimens (CCR)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	80	36		
Units: units on a scale				
arithmetic mean (standard deviation)	7.8 (± 27.28)	10.4 (± 23.09)		

Statistical analyses

No statistical analyses for this end point

Secondary: HRQoL: Change from Baseline in the EORTC QLQ-C30 Global Health Status-/Quality of Life Domain

End point title	HRQoL: Change from Baseline in the EORTC QLQ-C30 Global Health Status-/Quality of Life Domain

End point description:

The European Organization for Research and Treatment of Cancer (EORTC) Core Quality of Life (QOL) questionnaire (EORTC QLQ-C30) is a 30-question tool used to assess the overall QOL in cancer patients. It consists of 15 domains: 1 global health status (GHS) scale, 5 functional scales (Physical, Role, Cognitive, Emotional, Social), and 9 symptom scales/items (Fatigue, Nausea and Vomiting, Pain, Dyspnea, Sleep Disturbance, Appetite Loss, Constipation, Diarrhea, Financial Impact). The EORTC QLQ-C30 Global Health Status/QOL scale is scored between 0 and 100, with a high score indicating better Global Health Status/QOL. Negative change from Baseline values indicate deterioration in Global Health Status/QOL and positive values indicate improvement. The HRQoL Evaluable population included only participants with a baseline QoL assessment and at least 1 follow-up assessment. Time windows were applied post-hoc to increase the size of the analyzable population.

End point type	Secondary

End point timeframe:

Baseline to end of study, at approximately 11-12 months

End point values	Azacitidine (AZA)	Conventional Care Regimens (CCR)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	87	80		
Units: units on a scale				
arithmetic mean (standard deviation)	-4.4 (± 29.2)	-6.1 (± 27.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Healthcare Resource Utilization (HRU): Number of subjects with a hospitalization

End point title	Healthcare Resource Utilization (HRU): Number of subjects with a hospitalization

End point description:

HRU was defined as any consumption of healthcare resources directly or indirectly related to the treatment of the patient. HRU Analysis may help in evaluating potential costs and budget impact of new treatments from a payer perspective. HRU was analyzed for the HRQoL Evaluable Population, a smaller sample than either the ITT population or safety population. Duration of therapy differed between treatment groups.

End point type	Secondary

End point timeframe:

Day 1 (randomization) to 40 months

End point values	Azacitidine (AZA)	Conventional Care Regimens (CCR)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	157	134		
Units: participants	139	111		

Statistical analyses

No statistical analyses for this end point

Secondary: Healthcare Resource Utilization (HRU): Rate of Inpatient Hospitalizations Per Year

End point title	Healthcare Resource Utilization (HRU): Rate of Inpatient Hospitalizations Per Year

End point description:

HRU was defined as any consumption of healthcare resources directly or indirectly related to the treatment of the patient. HRU Analysis may help in evaluating potential costs and budget impact of new treatments from a payer perspective. The rate of inpatient hospitalizations per patient year was calculated as the total number of hospitalizations divided by the total number of patient-years followed in the study period. Patient-years (PY) were calculated as the duration from baseline to last available HRQL assessment for each patient.HRU was analyzed for the HRQoL Evaluable Population, a smaller sample than either the ITT population or safety population. Duration of therapy differed between

treatment groups. Rate-per-patient year values adjust for these differences.

End point type	Secondary

End point timeframe:

Day 1 (randomization) to 40 months

End point values	Azacitidine (AZA)	Conventional Care Regimens (CCR)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	157	134		
Units: hospitalizations per patient year				
number (not applicable)	7.95	4.82		

Statistical analyses

No statistical analyses for this end point

Secondary: HRU: Number of Subjects Receiving Transfusions

End point title	HRU: Number of Subjects Receiving Transfusions

End point description:

Count of study participants who had transfusions during the treatment phase. HRU is defined as any consumption of healthcare resources directly or indirectly related to the treatment of the patient. HRU Analysis may help in evaluating potential costs and budget impact of new treatments from a payer perspective. HRU was analyzed for the HRQoL Evaluable Population, a smaller sample than either the ITT population or safety population.

End point type	Secondary

End point timeframe:

Day 1 (randomization) to 40 months

End point values	Azacitidine (AZA)	Conventional Care Regimens (CCR)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	157	134		
Units: subjects	154	134		

Statistical analyses

No statistical analyses for this end point

Secondary: HRU: Rate of Transfusions per Patient Year

End point title	HRU: Rate of Transfusions per Patient Year

End point description:

HRU is defined as any consumption of healthcare resources directly or indirectly related to the treatment of the patient. HRU Analysis may help in evaluating potential costs and budget impact of new treatments from a payer perspective. The rate of transfusions per patient year was calculated as the total number of transfusions divided by the total number of patient-years followed in the study period. Patient-years (PY) were calculated as the duration from baseline to last available HRQL assessment for each patient. HRU was analyzed for the HRQoL Evaluable Population, a smaller sample than either the ITT population or safety population. Duration of therapy differed between treatment groups. Rate-per-patient year values adjust for these differences.

End point type	Secondary

End point timeframe:

Day 1 (randomization) to 40 months

End point values	Azacitidine (AZA)	Conventional Care Regimens (CCR)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	157	134		
Units: Transfusions per Patient Year				
number (not applicable)	34.23	36.04		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants in the Extension Phase With Treatment Emergent Adverse Events (TEAEs)

End point title	Number of Participants in the Extension Phase With Treatment Emergent Adverse Events (TEAEs)

End point description:

AEs = any noxious, unintended, or untoward medical occurrence that may appear or worsen during the course of a study. It may be a new intercurrent illness, a worsening concomitant illness, an injury, or any concomitant impairment of the participant's health, regardless of cause. Serious AE (SAE) = any AE which 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; constitutes an important medical event. The severity of AEs were graded based upon the participants symptoms according to the Common Terminology Criteria for Adverse Events (CTCAE, Version 4.0); AEs were evaluated for severity according to the following scale: Grade 1 = Mild – transient or mild discomfort; no medical intervention required; Grade 2 = Moderate – mild to moderate limitation in activity; Grade 3 = Severe; Grade 4 = Life threatening; Grade 5 = Death

End point type	Secondary

End point timeframe:

From the date of informed consent for the Extension Phase of the study through to the date of last dose of study drug + 28 days up to last visit completed 25 July 2016; maximum duration of exposure to Azacitidine in the extension phase was 871 days

End point values	Azacitidine (AZA)			
Subject group type	Reporting group			
Number of subjects analysed	22			
Units: participants				
At least one Treatment Emergent AE	20			
At least one TEAE related to study drug	13			
At least one Grade 3-4 adverse event	13			
At least 1 Grade 3-4 TEAE related to study drug	7			
At least 1 Grade 5 TEAE	4			
At least 1 Grade 5 TEAE related to study drug	0			
At least 1 serious TEAE	10			
At least 1 serious TEAE related to study drug	1			
At least one serious Grade 3-4 TEAE	8			
TEAE leading to discontinuation of study drug	3			
Study drug-related TEAE leading to discontinuation	1			
TEAE leading to study drug dose reduction	1			
TEAE leading to study drug dose interruption only	17			
TEAE causing study dose reduction/interruption	2			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From first dose to 1) last dose + 28 days for azacitidine and low-dose cytarabine; 2) last dose + 70 days for intensive chemotherapy; 3) discontinuation for BSC only;median duration was 191.5, 65.0, 125.0, 124.5 and 360.0 days for each group respectively

Adverse event reporting additional description:

Adverse Events reported for the Azacitidone treatment group are those that occurred in the treatment phase, adverse events reported in the Azacitidine extension group occurred during the extension phase

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	16.1

Reporting groups

Reporting group title	Azacitidine

Reporting group description:

Azacitidine 75 mg/m2/day by subcutaneous injection [SC] for 7 days every 28 days, with a 21 day rest period (optimally for at least 6 cycles) plus best supportive care as needed, including antibiotics and blood product transfusions, growth factors, per physician's discretion.

Reporting group title	BSC Only

Reporting group description:

BSC only = transfusion of blood products, antibiotics, antifungals and nutritional supplements

Reporting group title	Low-dose Cytarabine

Reporting group description:

Low-dose cytarabine 20 mg subcutaneously twice a day (BID) for 10 days every 28 days, plus BSC

Reporting group title	Intensive Chemotherapy

Reporting group description:

Intensive Chemotherapy: Cytarabine 100-200 mg/m2 as a continuous intravenous infusion (CIVI) for 7 days and daunorubicin 45 to 60 mg/m2 daily (QD) IV on Days 1, 2 and 3 or Idarubicin 9-12 mg/m2 IV QD for 3 days. Consolidation Therapy (Cycle 2 and 3) = Cytarabine 100-200 mg/m2 as a CIVI for 3 to 7 days and daunorubicin 45 to 60 mg/m2 QD or Idarubicin 9-12 mg/m2 IV QD on Days 1 and 2. The first consolidation therapy started between Day 28 and Day 70 from start of induction therapy, upon recovery of absolute neutrophil count (ANC) above 1.0 x 10^9/L and platelets above 75 x 10^9/L. The second cycle started between Day 28 and Day 70 from start of first consolidation therapy. Best supportive care (BSC) of antibiotics and transfusions, were given as needed

Reporting group title	Azacitidine-extension

Reporting group description:

Azacitidine 75 mg/m2/day by subcutaneous injection [SC] for 7 days every 28 days, with a 21 day rest period (optimally for at least 6 cycles) plus best supportive care as needed, including antibiotics and blood product transfusions, growth factors, per physician's discretion.

Serious adverse events	Azacitidine	BSC Only	Low-dose Cytarabine
Total subjects affected by serious adverse events			
subjects affected / exposed	188 / 236 (79.66%)	30 / 40 (75.00%)	118 / 153 (77.12%)
number of deaths (all causes)	56	23	38
number of deaths resulting from adverse events	12	0	10
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			

ACUTE MYELOID LEUKAEMIA			
subjects affected / exposed	26 / 236 (11.02%)	12 / 40 (30.00%)	17 / 153 (11.11%)
occurrences causally related to treatment / all	1 / 34	0 / 17	2 / 22
deaths causally related to treatment / all	0 / 12	0 / 10	1 / 10
CHLOROMA			
subjects affected / exposed	2 / 236 (0.85%)	0 / 40 (0.00%)	0 / 153 (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
LEUKAEMIC INFILTRATION BRAIN			
subjects affected / exposed	0 / 236 (0.00%)	0 / 40 (0.00%)	1 / 153 (0.65%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
OVARIAN CANCER METASTATIC			
subjects affected / exposed	1 / 236 (0.42%)	0 / 40 (0.00%)	0 / 153 (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 FLARE			
subjects affected / exposed	1 / 236 (0.42%)	0 / 40 (0.00%)	0 / 153 (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			
DEEP VEIN THROMBOSIS			
subjects affected / exposed	2 / 236 (0.85%)	1 / 40 (2.50%)	0 / 153 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HAEMATOMA			
subjects affected / exposed	2 / 236 (0.85%)	0 / 40 (0.00%)	0 / 153 (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
HYPERTENSION			
subjects affected / exposed	1 / 236 (0.42%)	0 / 40 (0.00%)	0 / 153 (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
HYPOTENSION			

subjects affected / exposed	4 / 236 (1.69%)	1 / 40 (2.50%)	0 / 153 (0.00%)
occurrences causally related to treatment / all	2 / 4	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
PERIPHERAL ISCHAEMIA			
subjects affected / exposed	1 / 236 (0.42%)	0 / 40 (0.00%)	0 / 153 (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
PHLEBITIS			
subjects affected / exposed	1 / 236 (0.42%)	0 / 40 (0.00%)	0 / 153 (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
THROMBOPHLEBITIS SUPERFICIAL			
subjects affected / exposed	1 / 236 (0.42%)	0 / 40 (0.00%)	0 / 153 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
ASTHENIA			
subjects affected / exposed	4 / 236 (1.69%)	1 / 40 (2.50%)	3 / 153 (1.96%)
occurrences causally related to treatment / all	3 / 4	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CHEST PAIN			
subjects affected / exposed	0 / 236 (0.00%)	0 / 40 (0.00%)	2 / 153 (1.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	3 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CHILLS			
subjects affected / exposed	1 / 236 (0.42%)	0 / 40 (0.00%)	1 / 153 (0.65%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DEATH			
subjects affected / exposed	3 / 236 (1.27%)	0 / 40 (0.00%)	2 / 153 (1.31%)
occurrences causally related to treatment / all	1 / 3	0 / 0	0 / 2
deaths causally related to treatment / all	1 / 3	0 / 0	0 / 2
FATIGUE			

subjects affected / exposed	3 / 236 (1.27%)	0 / 40 (0.00%)	1 / 153 (0.65%)
occurrences causally related to treatment / all	2 / 3	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GENERAL PHYSICAL HEALTH DETERIORATION			
subjects affected / exposed	1 / 236 (0.42%)	0 / 40 (0.00%)	1 / 153 (0.65%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPERTHERMIA			
subjects affected / exposed	1 / 236 (0.42%)	0 / 40 (0.00%)	0 / 153 (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
INJECTION SITE EXTRAVASATION			
subjects affected / exposed	1 / 236 (0.42%)	0 / 40 (0.00%)	0 / 153 (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
INJECTION SITE REACTION			
subjects affected / exposed	2 / 236 (0.85%)	0 / 40 (0.00%)	0 / 153 (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
MALAISE			
subjects affected / exposed	1 / 236 (0.42%)	0 / 40 (0.00%)	0 / 153 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MULTI-ORGAN FAILURE			
subjects affected / exposed	1 / 236 (0.42%)	0 / 40 (0.00%)	2 / 153 (1.31%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
OEDEMA PERIPHERAL			
subjects affected / exposed	0 / 236 (0.00%)	1 / 40 (2.50%)	0 / 153 (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
PAIN			

subjects affected / exposed	1 / 236 (0.42%)	0 / 40 (0.00%)	1 / 153 (0.65%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PYREXIA			
subjects affected / exposed	25 / 236 (10.59%)	3 / 40 (7.50%)	16 / 153 (10.46%)
occurrences causally related to treatment / all	13 / 35	0 / 3	7 / 21
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
SUDDEN CARDIAC DEATH			
subjects affected / exposed	1 / 236 (0.42%)	0 / 40 (0.00%)	1 / 153 (0.65%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	1 / 1
SUDDEN DEATH			
subjects affected / exposed	2 / 236 (0.85%)	0 / 40 (0.00%)	0 / 153 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 2	0 / 0	0 / 0
Immune system disorders			
ANAPHYLACTIC SHOCK			
subjects affected / exposed	1 / 236 (0.42%)	0 / 40 (0.00%)	0 / 153 (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, thoracic and mediastinal disorders			
ACUTE PULMONARY OEDEMA			
subjects affected / exposed	1 / 236 (0.42%)	0 / 40 (0.00%)	1 / 153 (0.65%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ACUTE RESPIRATORY DISTRESS SYNDROME			
subjects affected / exposed	1 / 236 (0.42%)	0 / 40 (0.00%)	0 / 153 (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 RESPIRATORY FAILURE			
subjects affected / exposed	2 / 236 (0.85%)	0 / 40 (0.00%)	0 / 153 (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

ASTHMA			
subjects affected / exposed	0 / 236 (0.00%)	1 / 40 (2.50%)	0 / 153 (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
CHRONIC OBSTRUCTIVE PULMONARY DISEASE			
subjects affected / exposed	0 / 236 (0.00%)	0 / 40 (0.00%)	1 / 153 (0.65%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DYSPNOEA			
subjects affected / exposed	5 / 236 (2.12%)	1 / 40 (2.50%)	3 / 153 (1.96%)
occurrences causally related to treatment / all	1 / 5	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
EPISTAXIS			
subjects affected / exposed	2 / 236 (0.85%)	0 / 40 (0.00%)	1 / 153 (0.65%)
occurrences causally related to treatment / all	0 / 2	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LUNG DISORDER			
subjects affected / exposed	1 / 236 (0.42%)	0 / 40 (0.00%)	2 / 153 (1.31%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ORGANISING PNEUMONIA			
subjects affected / exposed	1 / 236 (0.42%)	0 / 40 (0.00%)	0 / 153 (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
OROPHARYNGEAL PAIN			
subjects affected / exposed	1 / 236 (0.42%)	0 / 40 (0.00%)	0 / 153 (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	2 / 236 (0.85%)	0 / 40 (0.00%)	2 / 153 (1.31%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
PNEUMONIA ASPIRATION			

subjects affected / exposed	0 / 236 (0.00%)	1 / 40 (2.50%)	0 / 153 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
PNEUMONITIS			
subjects affected / exposed	1 / 236 (0.42%)	0 / 40 (0.00%)	1 / 153 (0.65%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PRODUCTIVE COUGH			
subjects affected / exposed	1 / 236 (0.42%)	0 / 40 (0.00%)	0 / 153 (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
PULMONARY ALVEOLAR HAEMORRHAGE			
subjects affected / exposed	1 / 236 (0.42%)	0 / 40 (0.00%)	0 / 153 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
PULMONARY EMBOLISM			
subjects affected / exposed	1 / 236 (0.42%)	0 / 40 (0.00%)	1 / 153 (0.65%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PULMONARY HAEMORRHAGE			
subjects affected / exposed	0 / 236 (0.00%)	1 / 40 (2.50%)	1 / 153 (0.65%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 1
PULMONARY OEDEMA			
subjects affected / exposed	2 / 236 (0.85%)	0 / 40 (0.00%)	2 / 153 (1.31%)
occurrences causally related to treatment / all	0 / 2	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RESPIRATORY FAILURE			
subjects affected / exposed	3 / 236 (1.27%)	1 / 40 (2.50%)	6 / 153 (3.92%)
occurrences causally related to treatment / all	3 / 4	0 / 1	3 / 7
deaths causally related to treatment / all	1 / 2	0 / 1	1 / 1
Psychiatric disorders			
CONFUSIONAL STATE			

subjects affected / exposed	1 / 236 (0.42%)	0 / 40 (0.00%)	0 / 153 (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			
TROPONIN INCREASED			
subjects affected / exposed	0 / 236 (0.00%)	0 / 40 (0.00%)	0 / 153 (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
URINE OUTPUT DECREASED			
subjects affected / exposed	0 / 236 (0.00%)	1 / 40 (2.50%)	0 / 153 (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
WEIGHT DECREASED			
subjects affected / exposed	0 / 236 (0.00%)	0 / 40 (0.00%)	1 / 153 (0.65%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
ALLERGIC TRANSFUSION REACTION			
subjects affected / exposed	0 / 236 (0.00%)	0 / 40 (0.00%)	1 / 153 (0.65%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ANKLE FRACTURE			
subjects affected / exposed	1 / 236 (0.42%)	0 / 40 (0.00%)	0 / 153 (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
CONCUSSION			
subjects affected / exposed	1 / 236 (0.42%)	0 / 40 (0.00%)	0 / 153 (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
CRANIOCEREBRAL INJURY			
subjects affected / exposed	1 / 236 (0.42%)	0 / 40 (0.00%)	0 / 153 (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

FALL			
subjects affected / exposed	2 / 236 (0.85%)	0 / 40 (0.00%)	0 / 153 (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
FEMUR FRACTURE			
subjects affected / exposed	1 / 236 (0.42%)	0 / 40 (0.00%)	1 / 153 (0.65%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HIP FRACTURE			
subjects affected / exposed	0 / 236 (0.00%)	0 / 40 (0.00%)	1 / 153 (0.65%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LIGAMENT SPRAIN			
subjects affected / exposed	1 / 236 (0.42%)	0 / 40 (0.00%)	0 / 153 (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
RIB FRACTURE			
subjects affected / exposed	1 / 236 (0.42%)	0 / 40 (0.00%)	0 / 153 (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
ROAD TRAFFIC ACCIDENT			
subjects affected / exposed	1 / 236 (0.42%)	0 / 40 (0.00%)	0 / 153 (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
SUBDURAL HAEMATOMA			
subjects affected / exposed	1 / 236 (0.42%)	0 / 40 (0.00%)	0 / 153 (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
TENDON RUPTURE			
subjects affected / exposed	1 / 236 (0.42%)	0 / 40 (0.00%)	0 / 153 (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 / 236 (0.42%)	0 / 40 (0.00%)	0 / 153 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
ACUTE CORONARY SYNDROME			
subjects affected / exposed	2 / 236 (0.85%)	0 / 40 (0.00%)	1 / 153 (0.65%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
ACUTE LEFT VENTRICULAR FAILURE			
subjects affected / exposed	1 / 236 (0.42%)	0 / 40 (0.00%)	0 / 153 (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	3 / 236 (1.27%)	0 / 40 (0.00%)	0 / 153 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
ANGINA PECTORIS			
subjects affected / exposed	0 / 236 (0.00%)	0 / 40 (0.00%)	1 / 153 (0.65%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ATRIAL FIBRILLATION			
subjects affected / exposed	7 / 236 (2.97%)	1 / 40 (2.50%)	3 / 153 (1.96%)
occurrences causally related to treatment / all	0 / 7	0 / 1	0 / 4
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
CARDIAC ARREST			
subjects affected / exposed	0 / 236 (0.00%)	0 / 40 (0.00%)	1 / 153 (0.65%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
CARDIAC FAILURE			
subjects affected / exposed	2 / 236 (0.85%)	0 / 40 (0.00%)	1 / 153 (0.65%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
CARDIAC FAILURE ACUTE			

subjects affected / exposed	0 / 236 (0.00%)	0 / 40 (0.00%)	0 / 153 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CARDIAC FAILURE CONGESTIVE			
subjects affected / exposed	0 / 236 (0.00%)	1 / 40 (2.50%)	0 / 153 (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
CARDIO-RESPIRATORY ARREST			
subjects affected / exposed	1 / 236 (0.42%)	0 / 40 (0.00%)	0 / 153 (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
CARDIOVASCULAR INSUFFICIENCY			
subjects affected / exposed	1 / 236 (0.42%)	0 / 40 (0.00%)	2 / 153 (1.31%)
occurrences causally related to treatment / all	1 / 1	0 / 0	2 / 2
deaths causally related to treatment / all	1 / 1	0 / 0	1 / 1
ISCHAEMIC CARDIOMYOPATHY			
subjects affected / exposed	1 / 236 (0.42%)	0 / 40 (0.00%)	0 / 153 (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
LEFT VENTRICULAR FAILURE			
subjects affected / exposed	1 / 236 (0.42%)	0 / 40 (0.00%)	0 / 153 (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
MYOCARDIAL INFARCTION			
subjects affected / exposed	0 / 236 (0.00%)	0 / 40 (0.00%)	1 / 153 (0.65%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
PERICARDIAL EFFUSION			
subjects affected / exposed	1 / 236 (0.42%)	0 / 40 (0.00%)	0 / 153 (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 / 236 (0.42%)	0 / 40 (0.00%)	1 / 153 (0.65%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SUPRAVENTRICULAR TACHYCARDIA			
subjects affected / exposed	0 / 236 (0.00%)	0 / 40 (0.00%)	1 / 153 (0.65%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VENTRICULAR TACHYCARDIA			
subjects affected / exposed	1 / 236 (0.42%)	0 / 40 (0.00%)	0 / 153 (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			
CEREBRAL HAEMORRHAGE			
subjects affected / exposed	1 / 236 (0.42%)	2 / 40 (5.00%)	0 / 153 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 2	0 / 0
CEREBRAL INFARCTION			
subjects affected / exposed	2 / 236 (0.85%)	0 / 40 (0.00%)	0 / 153 (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
CEREBROVASCULAR ACCIDENT			
subjects affected / exposed	1 / 236 (0.42%)	0 / 40 (0.00%)	2 / 153 (1.31%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
COGNITIVE DISORDER			
subjects affected / exposed	1 / 236 (0.42%)	0 / 40 (0.00%)	0 / 153 (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
CONVULSION			
subjects affected / exposed	1 / 236 (0.42%)	0 / 40 (0.00%)	0 / 153 (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
DIZZINESS			

subjects affected / exposed	5 / 236 (2.12%)	0 / 40 (0.00%)	0 / 153 (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
FEBRILE CONVULSION			
subjects affected / exposed	0 / 236 (0.00%)	1 / 40 (2.50%)	0 / 153 (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
HAEMORRHAGE INTRACRANIAL			
subjects affected / exposed	2 / 236 (0.85%)	0 / 40 (0.00%)	0 / 153 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
HEADACHE			
subjects affected / exposed	1 / 236 (0.42%)	0 / 40 (0.00%)	0 / 153 (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 / 236 (0.42%)	0 / 40 (0.00%)	0 / 153 (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
ORTHOSTATIC INTOLERANCE			
subjects affected / exposed	1 / 236 (0.42%)	0 / 40 (0.00%)	0 / 153 (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
PRESYNCOPE			
subjects affected / exposed	2 / 236 (0.85%)	1 / 40 (2.50%)	0 / 153 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SUBARACHNOID HAEMORRHAGE			
subjects affected / exposed	2 / 236 (0.85%)	0 / 40 (0.00%)	0 / 153 (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
SYNCOPE			

subjects affected / exposed	4 / 236 (1.69%)	0 / 40 (0.00%)	2 / 153 (1.31%)
occurrences causally related to treatment / all	1 / 5	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
TRANSIENT ISCHAEMIC ATTACK			
subjects affected / exposed	0 / 236 (0.00%)	0 / 40 (0.00%)	1 / 153 (0.65%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
AGRANULOCYTOSIS			
subjects affected / exposed	0 / 236 (0.00%)	0 / 40 (0.00%)	1 / 153 (0.65%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ANAEMIA			
subjects affected / exposed	10 / 236 (4.24%)	1 / 40 (2.50%)	11 / 153 (7.19%)
occurrences causally related to treatment / all	9 / 12	0 / 1	10 / 15
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DISSEMINATED INTRAVASCULAR COAGULATION			
subjects affected / exposed	1 / 236 (0.42%)	0 / 40 (0.00%)	0 / 153 (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
FEBRILE BONE MARROW APLASIA			
subjects affected / exposed	2 / 236 (0.85%)	0 / 40 (0.00%)	3 / 153 (1.96%)
occurrences causally related to treatment / all	0 / 3	0 / 0	3 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FEBRILE NEUTROPENIA			
subjects affected / exposed	59 / 236 (25.00%)	12 / 40 (30.00%)	38 / 153 (24.84%)
occurrences causally related to treatment / all	34 / 90	0 / 14	30 / 55
deaths causally related to treatment / all	0 / 2	0 / 0	0 / 0
LEUKOCYTOSIS			
subjects affected / exposed	4 / 236 (1.69%)	0 / 40 (0.00%)	1 / 153 (0.65%)
occurrences causally related to treatment / all	0 / 4	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LEUKOPENIA			

subjects affected / exposed	1 / 236 (0.42%)	0 / 40 (0.00%)	2 / 153 (1.31%)
occurrences causally related to treatment / all	1 / 1	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LYMPHADENOPATHY			
subjects affected / exposed	1 / 236 (0.42%)	0 / 40 (0.00%)	0 / 153 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NEUTROPENIA			
subjects affected / exposed	5 / 236 (2.12%)	1 / 40 (2.50%)	3 / 153 (1.96%)
occurrences causally related to treatment / all	4 / 5	0 / 1	2 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PANCYTOPENIA			
subjects affected / exposed	0 / 236 (0.00%)	0 / 40 (0.00%)	1 / 153 (0.65%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
THROMBOCYTOPENIA			
subjects affected / exposed	6 / 236 (2.54%)	0 / 40 (0.00%)	14 / 153 (9.15%)
occurrences causally related to treatment / all	4 / 7	0 / 0	12 / 17
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
THROMBOTIC THROMBOCYTOPENIC PURPURA			
subjects affected / exposed	1 / 236 (0.42%)	0 / 40 (0.00%)	0 / 153 (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
Eye disorders			
CATARACT			
subjects affected / exposed	1 / 236 (0.42%)	0 / 40 (0.00%)	0 / 153 (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
CONJUNCTIVAL HAEMORRHAGE			
subjects affected / exposed	1 / 236 (0.42%)	0 / 40 (0.00%)	0 / 153 (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 disorders			

ABDOMINAL PAIN			
subjects affected / exposed	1 / 236 (0.42%)	0 / 40 (0.00%)	1 / 153 (0.65%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ABDOMINAL PAIN LOWER			
subjects affected / exposed	0 / 236 (0.00%)	0 / 40 (0.00%)	2 / 153 (1.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ANAL HAEMORRHAGE			
subjects affected / exposed	0 / 236 (0.00%)	1 / 40 (2.50%)	1 / 153 (0.65%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ASCITES			
subjects affected / exposed	0 / 236 (0.00%)	0 / 40 (0.00%)	0 / 153 (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
COLITIS			
subjects affected / exposed	1 / 236 (0.42%)	0 / 40 (0.00%)	0 / 153 (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
CONSTIPATION			
subjects affected / exposed	0 / 236 (0.00%)	0 / 40 (0.00%)	0 / 153 (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
DIARRHOEA			
subjects affected / exposed	4 / 236 (1.69%)	0 / 40 (0.00%)	4 / 153 (2.61%)
occurrences causally related to treatment / all	2 / 4	0 / 0	4 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
DIVERTICULUM INTESTINAL			
subjects affected / exposed	1 / 236 (0.42%)	0 / 40 (0.00%)	0 / 153 (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
DUODENAL ULCER HAEMORRHAGE			

subjects affected / exposed	0 / 236 (0.00%)	0 / 40 (0.00%)	0 / 153 (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
DYSPHAGIA			
subjects affected / exposed	0 / 236 (0.00%)	0 / 40 (0.00%)	1 / 153 (0.65%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ENTERITIS			
subjects affected / exposed	0 / 236 (0.00%)	1 / 40 (2.50%)	0 / 153 (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
ENTEROCOLITIS			
subjects affected / exposed	1 / 236 (0.42%)	0 / 40 (0.00%)	0 / 153 (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
GASTRITIS			
subjects affected / exposed	1 / 236 (0.42%)	0 / 40 (0.00%)	0 / 153 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GASTROINTESTINAL HAEMORRHAGE			
subjects affected / exposed	1 / 236 (0.42%)	1 / 40 (2.50%)	4 / 153 (2.61%)
occurrences causally related to treatment / all	0 / 2	0 / 1	1 / 4
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 0
HAEMATEMESIS			
subjects affected / exposed	1 / 236 (0.42%)	0 / 40 (0.00%)	0 / 153 (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
ILEUS			
subjects affected / exposed	1 / 236 (0.42%)	0 / 40 (0.00%)	0 / 153 (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
INTESTINAL ISCHAEMIA			

subjects affected / exposed	0 / 236 (0.00%)	0 / 40 (0.00%)	0 / 153 (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
INTESTINAL OBSTRUCTION			
subjects affected / exposed	1 / 236 (0.42%)	0 / 40 (0.00%)	0 / 153 (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
MELAENA			
subjects affected / exposed	1 / 236 (0.42%)	0 / 40 (0.00%)	1 / 153 (0.65%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MOUTH HAEMORRHAGE			
subjects affected / exposed	1 / 236 (0.42%)	1 / 40 (2.50%)	0 / 153 (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
NAUSEA			
subjects affected / exposed	2 / 236 (0.85%)	0 / 40 (0.00%)	0 / 153 (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
RECTAL HAEMORRHAGE			
subjects affected / exposed	1 / 236 (0.42%)	0 / 40 (0.00%)	1 / 153 (0.65%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RECTAL ULCER			
subjects affected / exposed	1 / 236 (0.42%)	0 / 40 (0.00%)	0 / 153 (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	1 / 236 (0.42%)	0 / 40 (0.00%)	0 / 153 (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 GASTROINTESTINAL HAEMORRHAGE			

subjects affected / exposed	1 / 236 (0.42%)	0 / 40 (0.00%)	0 / 153 (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
VOMITING			
subjects affected / exposed	2 / 236 (0.85%)	0 / 40 (0.00%)	0 / 153 (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
Hepatobiliary disorders			
CHOLANGITIS			
subjects affected / exposed	1 / 236 (0.42%)	0 / 40 (0.00%)	0 / 153 (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
CHOLECYSTITIS			
subjects affected / exposed	1 / 236 (0.42%)	0 / 40 (0.00%)	0 / 153 (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
CHOLECYSTITIS ACUTE			
subjects affected / exposed	1 / 236 (0.42%)	0 / 40 (0.00%)	1 / 153 (0.65%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CHOLELITHIASIS			
subjects affected / exposed	1 / 236 (0.42%)	0 / 40 (0.00%)	0 / 153 (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 FAILURE			
subjects affected / exposed	0 / 236 (0.00%)	0 / 40 (0.00%)	2 / 153 (1.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPERBILIRUBINAEMIA			
subjects affected / exposed	0 / 236 (0.00%)	0 / 40 (0.00%)	0 / 153 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			

SKIN ULCER			
subjects affected / exposed	1 / 236 (0.42%)	0 / 40 (0.00%)	0 / 153 (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			
BLADDER MASS			
subjects affected / exposed	1 / 236 (0.42%)	0 / 40 (0.00%)	0 / 153 (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
HAEMATURIA			
subjects affected / exposed	0 / 236 (0.00%)	1 / 40 (2.50%)	0 / 153 (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 COLIC			
subjects affected / exposed	0 / 236 (0.00%)	0 / 40 (0.00%)	1 / 153 (0.65%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RENAL FAILURE			
subjects affected / exposed	3 / 236 (1.27%)	0 / 40 (0.00%)	2 / 153 (1.31%)
occurrences causally related to treatment / all	2 / 4	0 / 0	0 / 2
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
RENAL FAILURE ACUTE			
subjects affected / exposed	3 / 236 (1.27%)	0 / 40 (0.00%)	2 / 153 (1.31%)
occurrences causally related to treatment / all	0 / 4	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
RENAL FAILURE CHRONIC			
subjects affected / exposed	0 / 236 (0.00%)	1 / 40 (2.50%)	0 / 153 (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	0 / 236 (0.00%)	1 / 40 (2.50%)	0 / 153 (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 TUBULAR NECROSIS			

subjects affected / exposed	1 / 236 (0.42%)	0 / 40 (0.00%)	0 / 153 (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
URINARY RETENTION			
subjects affected / exposed	0 / 236 (0.00%)	0 / 40 (0.00%)	1 / 153 (0.65%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
ARTHRALGIA			
subjects affected / exposed	2 / 236 (0.85%)	0 / 40 (0.00%)	0 / 153 (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
ARTHRITIS			
subjects affected / exposed	1 / 236 (0.42%)	0 / 40 (0.00%)	0 / 153 (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	3 / 236 (1.27%)	0 / 40 (0.00%)	1 / 153 (0.65%)
occurrences causally related to treatment / all	1 / 3	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BONE PAIN			
subjects affected / exposed	1 / 236 (0.42%)	0 / 40 (0.00%)	0 / 153 (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
HAEMARTHROSIS			
subjects affected / exposed	0 / 236 (0.00%)	0 / 40 (0.00%)	1 / 153 (0.65%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MUSCULAR WEAKNESS			
subjects affected / exposed	2 / 236 (0.85%)	0 / 40 (0.00%)	0 / 153 (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
MYALGIA			

subjects affected / exposed	1 / 236 (0.42%)	0 / 40 (0.00%)	0 / 153 (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
OSTEOARTHRITIS			
subjects affected / exposed	0 / 236 (0.00%)	0 / 40 (0.00%)	0 / 153 (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
PAIN IN EXTREMITY			
subjects affected / exposed	0 / 236 (0.00%)	1 / 40 (2.50%)	0 / 153 (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
SPINAL OSTEOARTHRITIS			
subjects affected / exposed	0 / 236 (0.00%)	0 / 40 (0.00%)	1 / 153 (0.65%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
ABSCESS NECK			
subjects affected / exposed	1 / 236 (0.42%)	0 / 40 (0.00%)	0 / 153 (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
ABSCESS SOFT TISSUE			
subjects affected / exposed	1 / 236 (0.42%)	0 / 40 (0.00%)	0 / 153 (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 SINUSITIS			
subjects affected / exposed	1 / 236 (0.42%)	0 / 40 (0.00%)	0 / 153 (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
AEROMONA INFECTION			
subjects affected / exposed	0 / 236 (0.00%)	0 / 40 (0.00%)	1 / 153 (0.65%)
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	1 / 236 (0.42%)	0 / 40 (0.00%)	0 / 153 (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
APPENDICITIS			
subjects affected / exposed	1 / 236 (0.42%)	0 / 40 (0.00%)	0 / 153 (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
ARTHRITIS INFECTIVE			
subjects affected / exposed	1 / 236 (0.42%)	0 / 40 (0.00%)	0 / 153 (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
ASPERGILLUS INFECTION			
subjects affected / exposed	0 / 236 (0.00%)	1 / 40 (2.50%)	0 / 153 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
BACTERAEMIA			
subjects affected / exposed	2 / 236 (0.85%)	0 / 40 (0.00%)	1 / 153 (0.65%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BRONCHITIS			
subjects affected / exposed	3 / 236 (1.27%)	0 / 40 (0.00%)	1 / 153 (0.65%)
occurrences causally related to treatment / all	2 / 4	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BRONCHOPNEUMONIA			
subjects affected / exposed	4 / 236 (1.69%)	1 / 40 (2.50%)	1 / 153 (0.65%)
occurrences causally related to treatment / all	2 / 4	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
BRONCHOPULMONARY ASPERGILLOSIS			
subjects affected / exposed	3 / 236 (1.27%)	1 / 40 (2.50%)	0 / 153 (0.00%)
occurrences causally related to treatment / all	1 / 4	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CANDIDA INFECTION			

subjects affected / exposed	0 / 236 (0.00%)	0 / 40 (0.00%)	1 / 153 (0.65%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CELLULITIS			
subjects affected / exposed	5 / 236 (2.12%)	4 / 40 (10.00%)	3 / 153 (1.96%)
occurrences causally related to treatment / all	1 / 6	0 / 7	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
CELLULITIS ORBITAL			
subjects affected / exposed	1 / 236 (0.42%)	0 / 40 (0.00%)	0 / 153 (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 COLITIS			
subjects affected / exposed	2 / 236 (0.85%)	0 / 40 (0.00%)	1 / 153 (0.65%)
occurrences causally related to treatment / all	1 / 2	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CLOSTRIDIUM DIFFICILE INFECTION			
subjects affected / exposed	1 / 236 (0.42%)	0 / 40 (0.00%)	1 / 153 (0.65%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CORYNEBACTERIUM SEPSIS			
subjects affected / exposed	1 / 236 (0.42%)	0 / 40 (0.00%)	0 / 153 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CYSTITIS			
subjects affected / exposed	0 / 236 (0.00%)	0 / 40 (0.00%)	1 / 153 (0.65%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DEVICE RELATED INFECTION			
subjects affected / exposed	0 / 236 (0.00%)	0 / 40 (0.00%)	1 / 153 (0.65%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DEVICE RELATED SEPSIS			

subjects affected / exposed	2 / 236 (0.85%)	0 / 40 (0.00%)	0 / 153 (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
DIVERTICULITIS			
subjects affected / exposed	4 / 236 (1.69%)	0 / 40 (0.00%)	0 / 153 (0.00%)
occurrences causally related to treatment / all	2 / 6	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ENTEROBACTER PNEUMONIA			
subjects affected / exposed	1 / 236 (0.42%)	0 / 40 (0.00%)	0 / 153 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ENTEROCOCCAL BACTERAEMIA			
subjects affected / exposed	0 / 236 (0.00%)	1 / 40 (2.50%)	1 / 153 (0.65%)
occurrences causally related to treatment / all	0 / 0	0 / 1	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ENTEROCOCCAL SEPSIS			
subjects affected / exposed	1 / 236 (0.42%)	0 / 40 (0.00%)	0 / 153 (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
EPIGLOTTITIS			
subjects affected / exposed	1 / 236 (0.42%)	0 / 40 (0.00%)	0 / 153 (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
ERYSIPELAS			
subjects affected / exposed	1 / 236 (0.42%)	0 / 40 (0.00%)	0 / 153 (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
ESCHERICHIA BACTERAEMIA			
subjects affected / exposed	3 / 236 (1.27%)	0 / 40 (0.00%)	1 / 153 (0.65%)
occurrences causally related to treatment / all	0 / 3	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ESCHERICHIA INFECTION			

subjects affected / exposed	1 / 236 (0.42%)	0 / 40 (0.00%)	0 / 153 (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
ESCHERICHIA SEPSIS			
subjects affected / exposed	4 / 236 (1.69%)	0 / 40 (0.00%)	0 / 153 (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
FURUNCLE			
subjects affected / exposed	1 / 236 (0.42%)	0 / 40 (0.00%)	0 / 153 (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
GASTROENTERITIS			
subjects affected / exposed	1 / 236 (0.42%)	0 / 40 (0.00%)	1 / 153 (0.65%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GASTROENTERITIS CLOSTRIDIAL			
subjects affected / exposed	1 / 236 (0.42%)	0 / 40 (0.00%)	0 / 153 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GASTROINTESTINAL FUNGAL INFECTION			
subjects affected / exposed	0 / 236 (0.00%)	0 / 40 (0.00%)	1 / 153 (0.65%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GROIN ABSCESS			
subjects affected / exposed	1 / 236 (0.42%)	0 / 40 (0.00%)	0 / 153 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HERPES ZOSTER			
subjects affected / exposed	1 / 236 (0.42%)	0 / 40 (0.00%)	0 / 153 (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
INFECTED CYST			

subjects affected / exposed	1 / 236 (0.42%)	0 / 40 (0.00%)	0 / 153 (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
INFECTION			
subjects affected / exposed	0 / 236 (0.00%)	0 / 40 (0.00%)	1 / 153 (0.65%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INFECTIVE EXACERBATION OF CHRONIC OBSTRUCTIVE AIRWAYS DISEASE			
subjects affected / exposed	0 / 236 (0.00%)	0 / 40 (0.00%)	1 / 153 (0.65%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
KLEBSIELLA BACTERAEMIA			
subjects affected / exposed	0 / 236 (0.00%)	0 / 40 (0.00%)	1 / 153 (0.65%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
KLEBSIELLA SEPSIS			
subjects affected / exposed	1 / 236 (0.42%)	0 / 40 (0.00%)	0 / 153 (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 ABSCESS			
subjects affected / exposed	0 / 236 (0.00%)	0 / 40 (0.00%)	0 / 153 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LOBAR PNEUMONIA			
subjects affected / exposed	2 / 236 (0.85%)	0 / 40 (0.00%)	2 / 153 (1.31%)
occurrences causally related to treatment / all	1 / 2	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LOWER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	1 / 236 (0.42%)	1 / 40 (2.50%)	1 / 153 (0.65%)
occurrences causally related to treatment / all	0 / 1	0 / 2	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
LUNG ABSCESS			

subjects affected / exposed	1 / 236 (0.42%)	0 / 40 (0.00%)	0 / 153 (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
LUNG INFECTION			
subjects affected / exposed	2 / 236 (0.85%)	0 / 40 (0.00%)	1 / 153 (0.65%)
occurrences causally related to treatment / all	0 / 3	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MUMPS			
subjects affected / exposed	1 / 236 (0.42%)	0 / 40 (0.00%)	0 / 153 (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
NASOPHARYNGITIS			
subjects affected / exposed	1 / 236 (0.42%)	0 / 40 (0.00%)	0 / 153 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NEUTROPENIC SEPSIS			
subjects affected / exposed	7 / 236 (2.97%)	2 / 40 (5.00%)	4 / 153 (2.61%)
occurrences causally related to treatment / all	0 / 12	0 / 3	0 / 7
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
ORAL CANDIDIASIS			
subjects affected / exposed	1 / 236 (0.42%)	0 / 40 (0.00%)	0 / 153 (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
OROPHARYNGITIS FUNGAL			
subjects affected / exposed	0 / 236 (0.00%)	0 / 40 (0.00%)	0 / 153 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PARAINFLUENZAE VIRUS INFECTION			
subjects affected / exposed	1 / 236 (0.42%)	0 / 40 (0.00%)	0 / 153 (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	0 / 236 (0.00%)	1 / 40 (2.50%)	0 / 153 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
PERIRECTAL ABSCESS			
subjects affected / exposed	1 / 236 (0.42%)	0 / 40 (0.00%)	0 / 153 (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
PERITONITIS			
subjects affected / exposed	0 / 236 (0.00%)	0 / 40 (0.00%)	1 / 153 (0.65%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PHARYNGITIS			
subjects affected / exposed	2 / 236 (0.85%)	0 / 40 (0.00%)	2 / 153 (1.31%)
occurrences causally related to treatment / all	1 / 2	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PHARYNGOTONSILLITIS			
subjects affected / exposed	1 / 236 (0.42%)	0 / 40 (0.00%)	0 / 153 (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			
subjects affected / exposed	48 / 236 (20.34%)	3 / 40 (7.50%)	29 / 153 (18.95%)
occurrences causally related to treatment / all	31 / 81	0 / 6	15 / 42
deaths causally related to treatment / all	8 / 15	0 / 3	1 / 6
PNEUMONIA FUNGAL			
subjects affected / exposed	3 / 236 (1.27%)	0 / 40 (0.00%)	1 / 153 (0.65%)
occurrences causally related to treatment / all	2 / 3	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PNEUMONIA KLEBSIELLA			
subjects affected / exposed	0 / 236 (0.00%)	0 / 40 (0.00%)	1 / 153 (0.65%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PNEUMONIA MYCOPLASMAL			

subjects affected / exposed	1 / 236 (0.42%)	0 / 40 (0.00%)	0 / 153 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
PNEUMONIA PARAINFLUENZAE VIRAL			
subjects affected / exposed	1 / 236 (0.42%)	0 / 40 (0.00%)	0 / 153 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PNEUMONIA PSEUDOMONAS AERUGINOSA			
subjects affected / exposed	1 / 236 (0.42%)	0 / 40 (0.00%)	0 / 153 (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 STAPHYLOCOCCAL			
subjects affected / exposed	0 / 236 (0.00%)	0 / 40 (0.00%)	1 / 153 (0.65%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PNEUMONIA STREPTOCOCCAL			
subjects affected / exposed	0 / 236 (0.00%)	0 / 40 (0.00%)	0 / 153 (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
PSEUDOMEMBRANOUS COLITIS			
subjects affected / exposed	3 / 236 (1.27%)	0 / 40 (0.00%)	1 / 153 (0.65%)
occurrences causally related to treatment / all	1 / 4	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
PSEUDOMONAL BACTERAEMIA			
subjects affected / exposed	0 / 236 (0.00%)	0 / 40 (0.00%)	1 / 153 (0.65%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PSEUDOMONAL SEPSIS			
subjects affected / exposed	3 / 236 (1.27%)	0 / 40 (0.00%)	2 / 153 (1.31%)
occurrences causally related to treatment / all	1 / 3	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RESPIRATORY TRACT INFECTION			

subjects affected / exposed	0 / 236 (0.00%)	2 / 40 (5.00%)	2 / 153 (1.31%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 1
SEPSIS			
subjects affected / exposed	12 / 236 (5.08%)	1 / 40 (2.50%)	9 / 153 (5.88%)
occurrences causally related to treatment / all	4 / 14	0 / 1	5 / 12
deaths causally related to treatment / all	0 / 2	0 / 0	1 / 4
SEPTIC SHOCK			
subjects affected / exposed	4 / 236 (1.69%)	1 / 40 (2.50%)	4 / 153 (2.61%)
occurrences causally related to treatment / all	1 / 5	0 / 2	2 / 5
deaths causally related to treatment / all	0 / 3	0 / 1	1 / 3
SINUSITIS			
subjects affected / exposed	3 / 236 (1.27%)	0 / 40 (0.00%)	0 / 153 (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
SINUSITIS FUNGAL			
subjects affected / exposed	0 / 236 (0.00%)	0 / 40 (0.00%)	0 / 153 (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
SOFT TISSUE INFECTION			
subjects affected / exposed	1 / 236 (0.42%)	0 / 40 (0.00%)	0 / 153 (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 BACTERAEMIA			
subjects affected / exposed	1 / 236 (0.42%)	0 / 40 (0.00%)	0 / 153 (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	0 / 236 (0.00%)	0 / 40 (0.00%)	0 / 153 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SYSTEMIC CANDIDA			

subjects affected / exposed	0 / 236 (0.00%)	0 / 40 (0.00%)	0 / 153 (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
TONSILLITIS			
subjects affected / exposed	0 / 236 (0.00%)	0 / 40 (0.00%)	2 / 153 (1.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
TOOTH INFECTION			
subjects affected / exposed	2 / 236 (0.85%)	0 / 40 (0.00%)	0 / 153 (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 RESPIRATORY TRACT INFECTION			
subjects affected / exposed	2 / 236 (0.85%)	0 / 40 (0.00%)	0 / 153 (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
URINARY TRACT INFECTION			
subjects affected / exposed	7 / 236 (2.97%)	1 / 40 (2.50%)	3 / 153 (1.96%)
occurrences causally related to treatment / all	1 / 7	0 / 1	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
UROSEPSIS			
subjects affected / exposed	2 / 236 (0.85%)	0 / 40 (0.00%)	0 / 153 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
VAGINITIS GARDNERELLA			
subjects affected / exposed	0 / 236 (0.00%)	0 / 40 (0.00%)	1 / 153 (0.65%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VULVAL ABSCESS			
subjects affected / exposed	1 / 236 (0.42%)	0 / 40 (0.00%)	0 / 153 (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
ZYGOMYCOSIS			

subjects affected / exposed	0 / 236 (0.00%)	0 / 40 (0.00%)	0 / 153 (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			
CACHEXIA			
subjects affected / exposed	1 / 236 (0.42%)	0 / 40 (0.00%)	2 / 153 (1.31%)
occurrences causally related to treatment / all	0 / 1	0 / 0	3 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
DECREASED APPETITE			
subjects affected / exposed	0 / 236 (0.00%)	0 / 40 (0.00%)	0 / 153 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DEHYDRATION			
subjects affected / exposed	3 / 236 (1.27%)	0 / 40 (0.00%)	0 / 153 (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
FAILURE TO THRIVE			
subjects affected / exposed	0 / 236 (0.00%)	0 / 40 (0.00%)	1 / 153 (0.65%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FLUID OVERLOAD			
subjects affected / exposed	1 / 236 (0.42%)	0 / 40 (0.00%)	0 / 153 (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
HYPERGLYCAEMIA			
subjects affected / exposed	0 / 236 (0.00%)	1 / 40 (2.50%)	0 / 153 (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
HYPOKALAEMIA			
subjects affected / exposed	2 / 236 (0.85%)	0 / 40 (0.00%)	0 / 153 (0.00%)
occurrences causally related to treatment / all	0 / 9	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
HYPONATRAEMIA			

subjects affected / exposed	2 / 236 (0.85%)	0 / 40 (0.00%)	0 / 153 (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
TUMOUR LYSIS SYNDROME			
subjects affected / exposed	0 / 236 (0.00%)	0 / 40 (0.00%)	1 / 153 (0.65%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Intensive Chemotherapy	Azacitidine-extension	
Total subjects affected by serious adverse events			
subjects affected / exposed	27 / 42 (64.29%)	10 / 22 (45.45%)	
number of deaths (all causes)	9	4	
number of deaths resulting from adverse events	4	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
ACUTE MYELOID LEUKAEMIA			
subjects affected / exposed	0 / 42 (0.00%)	1 / 22 (4.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
CHLOROMA			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
LEUKAEMIC INFILTRATION BRAIN			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
OVARIAN CANCER METASTATIC			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
TUMOUR FLARE			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Vascular disorders			
DEEP VEIN THROMBOSIS			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
HAEMATOMA			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
HYPERTENSION			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (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 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PERIPHERAL ISCHAEMIA			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PHLEBITIS			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
THROMBOPHLEBITIS SUPERFICIAL			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
ASTHENIA			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

CHEST PAIN			
subjects affected / exposed	1 / 42 (2.38%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
CHILLS			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
DEATH			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (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	1 / 42 (2.38%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
GENERAL PHYSICAL HEALTH DETERIORATION			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
HYPERTHERMIA			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
INJECTION SITE EXTRAVASATION			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
INJECTION SITE REACTION			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (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 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
MULTI-ORGAN FAILURE			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
OEDEMA PERIPHERAL			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PAIN			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PYREXIA			
subjects affected / exposed	2 / 42 (4.76%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
SUDDEN CARDIAC DEATH			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
SUDDEN DEATH			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (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			
ANAPHYLACTIC SHOCK			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (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 PULMONARY OEDEMA			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ACUTE RESPIRATORY DISTRESS SYNDROME			
subjects affected / exposed	1 / 42 (2.38%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ACUTE RESPIRATORY FAILURE			
subjects affected / exposed	1 / 42 (2.38%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ASTHMA			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (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 / 42 (0.00%)	0 / 22 (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	1 / 42 (2.38%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
EPISTAXIS			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (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 / 42 (0.00%)	0 / 22 (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 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
OROPHARYNGEAL PAIN			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (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	1 / 42 (2.38%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PNEUMONIA ASPIRATION			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (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 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PRODUCTIVE COUGH			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PULMONARY ALVEOLAR HAEMORRHAGE			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PULMONARY EMBOLISM			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PULMONARY HAEMORRHAGE			

subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PULMONARY OEDEMA			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
RESPIRATORY FAILURE			
subjects affected / exposed	2 / 42 (4.76%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 2	0 / 0	
Psychiatric disorders			
CONFUSIONAL STATE			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
TROPONIN INCREASED			
subjects affected / exposed	1 / 42 (2.38%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
URINE OUTPUT DECREASED			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
WEIGHT DECREASED			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (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			
ALLERGIC TRANSFUSION REACTION			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (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 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
CONCUSSION			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
CRANIOCEREBRAL INJURY			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (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 / 42 (0.00%)	0 / 22 (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 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
HIP FRACTURE			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
LIGAMENT SPRAIN			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
RIB FRACTURE			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ROAD TRAFFIC ACCIDENT			

subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (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 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
TENDON RUPTURE			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (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 / 42 (0.00%)	0 / 22 (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 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ACUTE LEFT VENTRICULAR FAILURE			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (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	1 / 42 (2.38%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ANGINA PECTORIS			
subjects affected / exposed	0 / 42 (0.00%)	1 / 22 (4.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
ATRIAL FIBRILLATION			

subjects affected / exposed	2 / 42 (4.76%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	2 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
CARDIAC ARREST			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (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	1 / 42 (2.38%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
CARDIAC FAILURE ACUTE			
subjects affected / exposed	1 / 42 (2.38%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
CARDIAC FAILURE CONGESTIVE			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
CARDIO-RESPIRATORY ARREST			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
CARDIOVASCULAR INSUFFICIENCY			
subjects affected / exposed	1 / 42 (2.38%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
ISCHAEMIC CARDIOMYOPATHY			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
LEFT VENTRICULAR FAILURE			

subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
MYOCARDIAL INFARCTION			
subjects affected / exposed	0 / 42 (0.00%)	1 / 22 (4.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
PERICARDIAL EFFUSION			
subjects affected / exposed	1 / 42 (2.38%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PERICARDITIS			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
SUPRAVENTRICULAR TACHYCARDIA			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
VENTRICULAR TACHYCARDIA			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (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			
CEREBRAL HAEMORRHAGE			
subjects affected / exposed	1 / 42 (2.38%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
CEREBRAL INFARCTION			
subjects affected / exposed	0 / 42 (0.00%)	1 / 22 (4.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
CEREBROVASCULAR ACCIDENT			

subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
COGNITIVE DISORDER			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
CONVULSION			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
DIZZINESS			
subjects affected / exposed	0 / 42 (0.00%)	1 / 22 (4.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
FEBRILE CONVULSION			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (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 / 42 (2.38%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
HEADACHE			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (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 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ORTHOSTATIC INTOLERANCE			

subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PRESYNCOPE			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
SUBARACHNOID HAEMORRHAGE			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (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	1 / 42 (2.38%)	1 / 22 (4.55%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
TRANSIENT ISCHAEMIC ATTACK			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (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			
AGRANULOCYTOSIS			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (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	0 / 42 (0.00%)	1 / 22 (4.55%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
DISSEMINATED INTRAVASCULAR COAGULATION			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
FEBRILE BONE MARROW APLASIA			

subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
FEBRILE NEUTROPENIA			
subjects affected / exposed	7 / 42 (16.67%)	4 / 22 (18.18%)	
occurrences causally related to treatment / all	5 / 7	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 1	
LEUKOCYTOSIS			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
LEUKOPENIA			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
LYMPHADENOPATHY			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
NEUTROPENIA			
subjects affected / exposed	1 / 42 (2.38%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PANCYTOPENIA			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (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	0 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
THROMBOTIC THROMBOCYTOPENIC PURPURA			

subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
CATARACT			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
CONJUNCTIVAL HAEMORRHAGE			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
ABDOMINAL PAIN			
subjects affected / exposed	0 / 42 (0.00%)	1 / 22 (4.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
ABDOMINAL PAIN LOWER			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ANAL HAEMORRHAGE			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (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	1 / 42 (2.38%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
COLITIS			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (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 / 42 (0.00%)	1 / 22 (4.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
DIARRHOEA			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
DIVERTICULUM INTESTINAL			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
DUODENAL ULCER HAEMORRHAGE			
subjects affected / exposed	0 / 42 (0.00%)	1 / 22 (4.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
DYSPHAGIA			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ENTERITIS			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (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 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
GASTRITIS			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (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	0 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
HAEMATEMESIS			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ILEUS			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
INTESTINAL ISCHAEMIA			
subjects affected / exposed	0 / 42 (0.00%)	1 / 22 (4.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
INTESTINAL OBSTRUCTION			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
MELAENA			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (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 / 42 (0.00%)	0 / 22 (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 / 42 (0.00%)	0 / 22 (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 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
RECTAL ULCER			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
STOMATITIS			
subjects affected / exposed	0 / 42 (0.00%)	1 / 22 (4.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
UPPER GASTROINTESTINAL HAEMORRHAGE			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
VOMITING			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (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			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
CHOLECYSTITIS			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
CHOLECYSTITIS ACUTE			
subjects affected / exposed	1 / 42 (2.38%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
CHOLELITHIASIS			

subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
HEPATIC FAILURE			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (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 / 42 (0.00%)	1 / 22 (4.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
SKIN ULCER			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (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			
BLADDER MASS			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (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 / 42 (0.00%)	1 / 22 (4.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
RENAL COLIC			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (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 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
RENAL FAILURE ACUTE			

subjects affected / exposed	1 / 42 (2.38%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
RENAL FAILURE CHRONIC			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (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 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
RENAL TUBULAR NECROSIS			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
URINARY RETENTION			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
ARTHRALGIA			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ARTHRITIS			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (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 / 42 (0.00%)	0 / 22 (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 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
HAEMARTHROSIS			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (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 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
MYALGIA			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
OSTEOARTHRITIS			
subjects affected / exposed	0 / 42 (0.00%)	1 / 22 (4.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
PAIN IN EXTREMITY			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
SPINAL OSTEOARTHRITIS			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (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			
ABSCESS NECK			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ABSCESS SOFT TISSUE			

subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ACUTE SINUSITIS			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
AEROMONA INFECTION			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (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	0 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
APPENDICITIS			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ARTHRITIS INFECTIVE			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ASPERGILLUS INFECTION			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
BACTERAEMIA			
subjects affected / exposed	0 / 42 (0.00%)	1 / 22 (4.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
BRONCHITIS			

subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
BRONCHOPNEUMONIA			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (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 / 42 (0.00%)	1 / 22 (4.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
CANDIDA INFECTION			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (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	1 / 42 (2.38%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
CELLULITIS ORBITAL			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (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 / 42 (0.00%)	0 / 22 (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 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
CORYNEBACTERIUM SEPSIS			

subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
CYSTITIS			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (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	0 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
DEVICE RELATED SEPSIS			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
DIVERTICULITIS			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ENTEROBACTER PNEUMONIA			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ENTEROCOCCAL BACTERAEMIA			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ENTEROCOCCAL SEPSIS			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (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 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ERYSIPELAS			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ESCHERICHIA BACTERAEMIA			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ESCHERICHIA INFECTION			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (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 / 42 (0.00%)	0 / 22 (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 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
GASTROENTERITIS			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
GASTROENTERITIS CLOSTRIDIAL			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
GASTROINTESTINAL FUNGAL INFECTION			

subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
GROIN ABSCESS			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
HERPES ZOSTER			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
INFECTED CYST			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (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 / 42 (0.00%)	1 / 22 (4.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
INFECTIVE EXACERBATION OF CHRONIC OBSTRUCTIVE AIRWAYS DISEASE			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (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 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
KLEBSIELLA SEPSIS			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (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 / 42 (0.00%)	1 / 22 (4.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
LOBAR PNEUMONIA			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (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 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
LUNG ABSCESS			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
LUNG INFECTION			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
MUMPS			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
NASOPHARYNGITIS			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (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 / 42 (2.38%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ORAL CANDIDIASIS			

subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
OROPHARYNGITIS FUNGAL			
subjects affected / exposed	1 / 42 (2.38%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PARAINFLUENZAE VIRUS INFECTION			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (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 / 42 (0.00%)	0 / 22 (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 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PERITONITIS			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (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	0 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PHARYNGOTONSILLITIS			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PNEUMONIA			

subjects affected / exposed	3 / 42 (7.14%)	2 / 22 (9.09%)	
occurrences causally related to treatment / all	2 / 3	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
PNEUMONIA FUNGAL			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PNEUMONIA KLEBSIELLA			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PNEUMONIA MYCOPLASMAL			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PNEUMONIA PARAINFLUENZAE VIRAL			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PNEUMONIA PSEUDOMONAS AERUGINOSA			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PNEUMONIA STAPHYLOCOCCAL			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PNEUMONIA STREPTOCOCCAL			
subjects affected / exposed	1 / 42 (2.38%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PSEUDOMEMBRANOUS COLITIS			

subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PSEUDOMONAL BACTERAEMIA			
subjects affected / exposed	0 / 42 (0.00%)	1 / 22 (4.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
PSEUDOMONAL SEPSIS			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
RESPIRATORY TRACT INFECTION			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
SEPSIS			
subjects affected / exposed	2 / 42 (4.76%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
SEPTIC SHOCK			
subjects affected / exposed	4 / 42 (9.52%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	3 / 4	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
SINUSITIS			
subjects affected / exposed	0 / 42 (0.00%)	1 / 22 (4.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
SINUSITIS FUNGAL			
subjects affected / exposed	1 / 42 (2.38%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
SOFT TISSUE INFECTION			

subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (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 / 42 (2.38%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
STAPHYLOCOCCAL SEPSIS			
subjects affected / exposed	1 / 42 (2.38%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
SYSTEMIC CANDIDA			
subjects affected / exposed	0 / 42 (0.00%)	1 / 22 (4.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
TONSILLITIS			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
TOOTH INFECTION			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (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 / 42 (0.00%)	0 / 22 (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	0 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
UROSEPSIS			

subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
VAGINITIS GARDNERELLA			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
VULVAL ABSCESS			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ZYGOMYCOSIS			
subjects affected / exposed	1 / 42 (2.38%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
CACHEXIA			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (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 / 42 (0.00%)	1 / 22 (4.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
DEHYDRATION			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
FAILURE TO THRIVE			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
FLUID OVERLOAD			

subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
HYPERGLYCAEMIA			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (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	0 / 42 (0.00%)	0 / 22 (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 / 42 (0.00%)	0 / 22 (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 / 42 (0.00%)	0 / 22 (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	Azacitidine	BSC Only	Low-dose Cytarabine
Total subjects affected by non-serious adverse events			
subjects affected / exposed	226 / 236 (95.76%)	33 / 40 (82.50%)	151 / 153 (98.69%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
ACUTE MYELOID LEUKAEMIA			
subjects affected / exposed	27 / 236 (11.44%)	2 / 40 (5.00%)	21 / 153 (13.73%)
occurrences (all)	27	2	21
Vascular disorders			
HAEMATOMA			
subjects affected / exposed	16 / 236 (6.78%)	2 / 40 (5.00%)	7 / 153 (4.58%)
occurrences (all)	22	2	13
HYPERTENSION			

subjects affected / exposed	16 / 236 (6.78%)	1 / 40 (2.50%)	13 / 153 (8.50%)
occurrences (all)	23	1	27
HYPOTENSION			
subjects affected / exposed	19 / 236 (8.05%)	3 / 40 (7.50%)	14 / 153 (9.15%)
occurrences (all)	24	3	14
PHLEBITIS			
subjects affected / exposed	7 / 236 (2.97%)	2 / 40 (5.00%)	4 / 153 (2.61%)
occurrences (all)	7	2	5
General disorders and administration site conditions			
ASTHENIA			
subjects affected / exposed	53 / 236 (22.46%)	8 / 40 (20.00%)	32 / 153 (20.92%)
occurrences (all)	73	9	45
CATHETER SITE PAIN			
subjects affected / exposed	3 / 236 (1.27%)	0 / 40 (0.00%)	1 / 153 (0.65%)
occurrences (all)	3	0	1
CHILLS			
subjects affected / exposed	11 / 236 (4.66%)	1 / 40 (2.50%)	7 / 153 (4.58%)
occurrences (all)	12	1	13
FATIGUE			
subjects affected / exposed	53 / 236 (22.46%)	10 / 40 (25.00%)	19 / 153 (12.42%)
occurrences (all)	92	14	28
INJECTION SITE ERYTHEMA			
subjects affected / exposed	29 / 236 (12.29%)	0 / 40 (0.00%)	0 / 153 (0.00%)
occurrences (all)	73	0	0
INJECTION SITE PAIN			
subjects affected / exposed	12 / 236 (5.08%)	0 / 40 (0.00%)	1 / 153 (0.65%)
occurrences (all)	16	0	2
INJECTION SITE REACTION			
subjects affected / exposed	30 / 236 (12.71%)	0 / 40 (0.00%)	0 / 153 (0.00%)
occurrences (all)	47	0	0
MALAISE			
subjects affected / exposed	7 / 236 (2.97%)	2 / 40 (5.00%)	3 / 153 (1.96%)
occurrences (all)	7	2	6
MUCOSAL INFLAMMATION			

subjects affected / exposed	8 / 236 (3.39%)	0 / 40 (0.00%)	14 / 153 (9.15%)
occurrences (all)	10	0	15
OEDEMA			
subjects affected / exposed	8 / 236 (3.39%)	0 / 40 (0.00%)	3 / 153 (1.96%)
occurrences (all)	8	0	3
OEDEMA PERIPHERAL			
subjects affected / exposed	55 / 236 (23.31%)	6 / 40 (15.00%)	33 / 153 (21.57%)
occurrences (all)	62	6	40
PAIN			
subjects affected / exposed	16 / 236 (6.78%)	5 / 40 (12.50%)	5 / 153 (3.27%)
occurrences (all)	17	5	5
PYREXIA			
subjects affected / exposed	77 / 236 (32.63%)	7 / 40 (17.50%)	56 / 153 (36.60%)
occurrences (all)	130	15	91
Respiratory, thoracic and mediastinal disorders			
COUGH			
subjects affected / exposed	54 / 236 (22.88%)	6 / 40 (15.00%)	36 / 153 (23.53%)
occurrences (all)	82	7	51
DYSPNOEA			
subjects affected / exposed	41 / 236 (17.37%)	6 / 40 (15.00%)	35 / 153 (22.88%)
occurrences (all)	54	7	46
DYSPNOEA EXERTIONAL			
subjects affected / exposed	10 / 236 (4.24%)	2 / 40 (5.00%)	6 / 153 (3.92%)
occurrences (all)	11	3	10
EPISTAXIS			
subjects affected / exposed	29 / 236 (12.29%)	5 / 40 (12.50%)	21 / 153 (13.73%)
occurrences (all)	50	8	39
HAEMOPTYSIS			
subjects affected / exposed	9 / 236 (3.81%)	2 / 40 (5.00%)	4 / 153 (2.61%)
occurrences (all)	11	2	4
HICCUPS			
subjects affected / exposed	0 / 236 (0.00%)	1 / 40 (2.50%)	0 / 153 (0.00%)
occurrences (all)	0	1	0
OROPHARYNGEAL PAIN			

subjects affected / exposed	16 / 236 (6.78%)	2 / 40 (5.00%)	11 / 153 (7.19%)
occurrences (all)	16	3	12
PLEURAL EFFUSION			
subjects affected / exposed	12 / 236 (5.08%)	1 / 40 (2.50%)	2 / 153 (1.31%)
occurrences (all)	14	1	4
PRODUCTIVE COUGH			
subjects affected / exposed	9 / 236 (3.81%)	0 / 40 (0.00%)	10 / 153 (6.54%)
occurrences (all)	15	0	12
Psychiatric disorders			
AGITATION			
subjects affected / exposed	6 / 236 (2.54%)	3 / 40 (7.50%)	3 / 153 (1.96%)
occurrences (all)	6	3	3
ANXIETY			
subjects affected / exposed	15 / 236 (6.36%)	4 / 40 (10.00%)	6 / 153 (3.92%)
occurrences (all)	15	5	6
CONFUSIONAL STATE			
subjects affected / exposed	14 / 236 (5.93%)	3 / 40 (7.50%)	8 / 153 (5.23%)
occurrences (all)	16	3	9
INSOMNIA			
subjects affected / exposed	36 / 236 (15.25%)	2 / 40 (5.00%)	11 / 153 (7.19%)
occurrences (all)	45	2	15
Investigations			
WEIGHT DECREASED			
subjects affected / exposed	30 / 236 (12.71%)	3 / 40 (7.50%)	2 / 153 (1.31%)
occurrences (all)	38	3	4
Injury, poisoning and procedural complications			
CONTUSION			
subjects affected / exposed	16 / 236 (6.78%)	3 / 40 (7.50%)	7 / 153 (4.58%)
occurrences (all)	24	4	10
FALL			
subjects affected / exposed	14 / 236 (5.93%)	2 / 40 (5.00%)	7 / 153 (4.58%)
occurrences (all)	21	2	9
LACERATION			
subjects affected / exposed	3 / 236 (1.27%)	0 / 40 (0.00%)	2 / 153 (1.31%)
occurrences (all)	3	0	2
Cardiac disorders			

ATRIAL FIBRILLATION			
subjects affected / exposed	12 / 236 (5.08%)	2 / 40 (5.00%)	9 / 153 (5.88%)
occurrences (all)	13	2	9
TACHYCARDIA			
subjects affected / exposed	5 / 236 (2.12%)	3 / 40 (7.50%)	2 / 153 (1.31%)
occurrences (all)	6	3	2
Nervous system disorders			
DIZZINESS			
subjects affected / exposed	42 / 236 (17.80%)	3 / 40 (7.50%)	15 / 153 (9.80%)
occurrences (all)	61	4	22
HEADACHE			
subjects affected / exposed	31 / 236 (13.14%)	1 / 40 (2.50%)	19 / 153 (12.42%)
occurrences (all)	48	1	34
SCIATICA			
subjects affected / exposed	4 / 236 (1.69%)	2 / 40 (5.00%)	2 / 153 (1.31%)
occurrences (all)	5	2	2
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	41 / 236 (17.37%)	3 / 40 (7.50%)	32 / 153 (20.92%)
occurrences (all)	135	3	134
FEBRILE NEUTROPENIA			
subjects affected / exposed	28 / 236 (11.86%)	2 / 40 (5.00%)	21 / 153 (13.73%)
occurrences (all)	37	2	30
LEUKOCYTOSIS			
subjects affected / exposed	13 / 236 (5.51%)	2 / 40 (5.00%)	11 / 153 (7.19%)
occurrences (all)	20	2	11
LEUKOPENIA			
subjects affected / exposed	22 / 236 (9.32%)	0 / 40 (0.00%)	15 / 153 (9.80%)
occurrences (all)	45	0	42
NEUTROPENIA			
subjects affected / exposed	69 / 236 (29.24%)	1 / 40 (2.50%)	43 / 153 (28.10%)
occurrences (all)	166	1	166
THROMBOCYTOPENIA			
subjects affected / exposed	60 / 236 (25.42%)	2 / 40 (5.00%)	37 / 153 (24.18%)
occurrences (all)	229	2	167
Gastrointestinal disorders			

ABDOMINAL DISTENSION			
subjects affected / exposed	3 / 236 (1.27%)	4 / 40 (10.00%)	4 / 153 (2.61%)
occurrences (all)	4	4	6
ABDOMINAL PAIN			
subjects affected / exposed	30 / 236 (12.71%)	3 / 40 (7.50%)	16 / 153 (10.46%)
occurrences (all)	39	3	34
ABDOMINAL PAIN UPPER			
subjects affected / exposed	19 / 236 (8.05%)	0 / 40 (0.00%)	6 / 153 (3.92%)
occurrences (all)	23	0	10
CONSTIPATION			
subjects affected / exposed	99 / 236 (41.95%)	9 / 40 (22.50%)	42 / 153 (27.45%)
occurrences (all)	172	12	58
DIARRHOEA			
subjects affected / exposed	87 / 236 (36.86%)	5 / 40 (12.50%)	34 / 153 (22.22%)
occurrences (all)	157	7	46
DYSPEPSIA			
subjects affected / exposed	16 / 236 (6.78%)	2 / 40 (5.00%)	14 / 153 (9.15%)
occurrences (all)	25	2	22
HAEMORRHOIDS			
subjects affected / exposed	14 / 236 (5.93%)	1 / 40 (2.50%)	7 / 153 (4.58%)
occurrences (all)	15	1	7
MOUTH ULCERATION			
subjects affected / exposed	11 / 236 (4.66%)	1 / 40 (2.50%)	8 / 153 (5.23%)
occurrences (all)	11	1	10
NAUSEA			
subjects affected / exposed	93 / 236 (39.41%)	3 / 40 (7.50%)	43 / 153 (28.10%)
occurrences (all)	158	3	69
STOMATITIS			
subjects affected / exposed	20 / 236 (8.47%)	2 / 40 (5.00%)	14 / 153 (9.15%)
occurrences (all)	31	2	21
VOMITING			
subjects affected / exposed	53 / 236 (22.46%)	3 / 40 (7.50%)	24 / 153 (15.69%)
occurrences (all)	86	4	40
Skin and subcutaneous tissue disorders			
ERYTHEMA			

subjects affected / exposed	18 / 236 (7.63%)	0 / 40 (0.00%)	6 / 153 (3.92%)
occurrences (all)	30	0	7
PETECHIAE			
subjects affected / exposed	12 / 236 (5.08%)	0 / 40 (0.00%)	16 / 153 (10.46%)
occurrences (all)	20	0	23
PRURITUS			
subjects affected / exposed	25 / 236 (10.59%)	1 / 40 (2.50%)	10 / 153 (6.54%)
occurrences (all)	33	1	10
RASH			
subjects affected / exposed	26 / 236 (11.02%)	0 / 40 (0.00%)	14 / 153 (9.15%)
occurrences (all)	36	0	18
SKIN LESION			
subjects affected / exposed	4 / 236 (1.69%)	2 / 40 (5.00%)	5 / 153 (3.27%)
occurrences (all)	5	2	5
SKIN ULCER			
subjects affected / exposed	7 / 236 (2.97%)	2 / 40 (5.00%)	2 / 153 (1.31%)
occurrences (all)	7	2	2
Renal and urinary disorders			
HAEMATURIA			
subjects affected / exposed	5 / 236 (2.12%)	3 / 40 (7.50%)	8 / 153 (5.23%)
occurrences (all)	5	3	8
RENAL FAILURE			
subjects affected / exposed	7 / 236 (2.97%)	2 / 40 (5.00%)	3 / 153 (1.96%)
occurrences (all)	8	2	3
RENAL FAILURE ACUTE			
subjects affected / exposed	4 / 236 (1.69%)	2 / 40 (5.00%)	3 / 153 (1.96%)
occurrences (all)	9	2	3
URINARY INCONTINENCE			
subjects affected / exposed	5 / 236 (2.12%)	2 / 40 (5.00%)	1 / 153 (0.65%)
occurrences (all)	6	2	1
Musculoskeletal and connective tissue disorders			
ARTHRALGIA			
subjects affected / exposed	33 / 236 (13.98%)	2 / 40 (5.00%)	11 / 153 (7.19%)
occurrences (all)	50	3	19
BACK PAIN			

subjects affected / exposed	36 / 236 (15.25%)	5 / 40 (12.50%)	22 / 153 (14.38%)
occurrences (all)	45	5	27
BONE PAIN			
subjects affected / exposed	12 / 236 (5.08%)	2 / 40 (5.00%)	4 / 153 (2.61%)
occurrences (all)	14	2	4
MUSCULOSKELETAL PAIN			
subjects affected / exposed	21 / 236 (8.90%)	2 / 40 (5.00%)	3 / 153 (1.96%)
occurrences (all)	27	2	3
PAIN IN EXTREMITY			
subjects affected / exposed	26 / 236 (11.02%)	2 / 40 (5.00%)	11 / 153 (7.19%)
occurrences (all)	35	3	11
Infections and infestations			
CELLULITIS			
subjects affected / exposed	13 / 236 (5.51%)	3 / 40 (7.50%)	7 / 153 (4.58%)
occurrences (all)	16	4	13
LUNG INFECTION			
subjects affected / exposed	1 / 236 (0.42%)	0 / 40 (0.00%)	3 / 153 (1.96%)
occurrences (all)	1	0	4
NASOPHARYNGITIS			
subjects affected / exposed	13 / 236 (5.51%)	2 / 40 (5.00%)	5 / 153 (3.27%)
occurrences (all)	17	2	5
ORAL CANDIDIASIS			
subjects affected / exposed	16 / 236 (6.78%)	4 / 40 (10.00%)	4 / 153 (2.61%)
occurrences (all)	21	4	5
ORAL HERPES			
subjects affected / exposed	15 / 236 (6.36%)	2 / 40 (5.00%)	8 / 153 (5.23%)
occurrences (all)	16	2	10
PHARYNGITIS			
subjects affected / exposed	9 / 236 (3.81%)	1 / 40 (2.50%)	5 / 153 (3.27%)
occurrences (all)	10	1	6
PNEUMONIA			
subjects affected / exposed	16 / 236 (6.78%)	0 / 40 (0.00%)	12 / 153 (7.84%)
occurrences (all)	17	0	13
RESPIRATORY TRACT INFECTION			
subjects affected / exposed	5 / 236 (2.12%)	2 / 40 (5.00%)	4 / 153 (2.61%)
occurrences (all)	6	2	4

SKIN INFECTION			
subjects affected / exposed	5 / 236 (2.12%)	0 / 40 (0.00%)	0 / 153 (0.00%)
occurrences (all)	7	0	0
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	18 / 236 (7.63%)	1 / 40 (2.50%)	5 / 153 (3.27%)
occurrences (all)	33	1	9
URINARY TRACT INFECTION			
subjects affected / exposed	16 / 236 (6.78%)	3 / 40 (7.50%)	14 / 153 (9.15%)
occurrences (all)	18	3	24
Metabolism and nutrition disorders			
DECREASED APPETITE			
subjects affected / exposed	61 / 236 (25.85%)	8 / 40 (20.00%)	33 / 153 (21.57%)
occurrences (all)	100	12	55
DEHYDRATION			
subjects affected / exposed	11 / 236 (4.66%)	2 / 40 (5.00%)	4 / 153 (2.61%)
occurrences (all)	13	2	4
FLUID OVERLOAD			
subjects affected / exposed	8 / 236 (3.39%)	2 / 40 (5.00%)	0 / 153 (0.00%)
occurrences (all)	10	2	0
FLUID RETENTION			
subjects affected / exposed	5 / 236 (2.12%)	0 / 40 (0.00%)	0 / 153 (0.00%)
occurrences (all)	5	0	0
HYPOALBUMINAEMIA			
subjects affected / exposed	11 / 236 (4.66%)	1 / 40 (2.50%)	11 / 153 (7.19%)
occurrences (all)	22	1	13
HYPOCALCAEMIA			
subjects affected / exposed	16 / 236 (6.78%)	0 / 40 (0.00%)	6 / 153 (3.92%)
occurrences (all)	22	0	11
HYPOKALAEMIA			
subjects affected / exposed	54 / 236 (22.88%)	6 / 40 (15.00%)	45 / 153 (29.41%)
occurrences (all)	103	8	79
HYPOMAGNESAEMIA			
subjects affected / exposed	21 / 236 (8.90%)	2 / 40 (5.00%)	9 / 153 (5.88%)
occurrences (all)	40	2	16
HYPONATRAEMIA			

subjects affected / exposed	9 / 236 (3.81%)	0 / 40 (0.00%)	12 / 153 (7.84%)
occurrences (all)	17	0	15
HYPOPHOSPHATAEMIA			
subjects affected / exposed	19 / 236 (8.05%)	2 / 40 (5.00%)	8 / 153 (5.23%)
occurrences (all)	34	2	9

Non-serious adverse events	Intensive Chemotherapy	Azacitidine-extension	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	42 / 42 (100.00%)	18 / 22 (81.82%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
ACUTE MYELOID LEUKAEMIA			
subjects affected / exposed	1 / 42 (2.38%)	0 / 22 (0.00%)	
occurrences (all)	1	0	
Vascular disorders			
HAEMATOMA			
subjects affected / exposed	1 / 42 (2.38%)	2 / 22 (9.09%)	
occurrences (all)	1	2	
HYPERTENSION			
subjects affected / exposed	4 / 42 (9.52%)	2 / 22 (9.09%)	
occurrences (all)	5	2	
HYPOTENSION			
subjects affected / exposed	1 / 42 (2.38%)	1 / 22 (4.55%)	
occurrences (all)	1	1	
PHLEBITIS			
subjects affected / exposed	2 / 42 (4.76%)	1 / 22 (4.55%)	
occurrences (all)	3	1	
General disorders and administration site conditions			
ASTHENIA			
subjects affected / exposed	5 / 42 (11.90%)	6 / 22 (27.27%)	
occurrences (all)	5	9	
CATHETER SITE PAIN			
subjects affected / exposed	3 / 42 (7.14%)	0 / 22 (0.00%)	
occurrences (all)	3	0	
CHILLS			
subjects affected / exposed	4 / 42 (9.52%)	0 / 22 (0.00%)	
occurrences (all)	7	0	

FATIGUE			
subjects affected / exposed	4 / 42 (9.52%)	3 / 22 (13.64%)	
occurrences (all)	4	4	
INJECTION SITE ERYTHEMA			
subjects affected / exposed	0 / 42 (0.00%)	1 / 22 (4.55%)	
occurrences (all)	0	1	
INJECTION SITE PAIN			
subjects affected / exposed	0 / 42 (0.00%)	1 / 22 (4.55%)	
occurrences (all)	0	3	
INJECTION SITE REACTION			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences (all)	0	0	
MALAISE			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences (all)	0	0	
MUCOSAL INFLAMMATION			
subjects affected / exposed	3 / 42 (7.14%)	0 / 22 (0.00%)	
occurrences (all)	4	0	
OEDEMA			
subjects affected / exposed	1 / 42 (2.38%)	2 / 22 (9.09%)	
occurrences (all)	1	3	
OEDEMA PERIPHERAL			
subjects affected / exposed	9 / 42 (21.43%)	2 / 22 (9.09%)	
occurrences (all)	11	2	
PAIN			
subjects affected / exposed	3 / 42 (7.14%)	2 / 22 (9.09%)	
occurrences (all)	3	4	
PYREXIA			
subjects affected / exposed	21 / 42 (50.00%)	4 / 22 (18.18%)	
occurrences (all)	42	6	
Respiratory, thoracic and mediastinal disorders			
COUGH			
subjects affected / exposed	6 / 42 (14.29%)	5 / 22 (22.73%)	
occurrences (all)	7	6	
DYSPNOEA			

subjects affected / exposed	4 / 42 (9.52%)	1 / 22 (4.55%)	
occurrences (all)	5	3	
DYSPNOEA EXERTIONAL			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences (all)	0	0	
EPISTAXIS			
subjects affected / exposed	2 / 42 (4.76%)	4 / 22 (18.18%)	
occurrences (all)	4	4	
HAEMOPTYSIS			
subjects affected / exposed	2 / 42 (4.76%)	0 / 22 (0.00%)	
occurrences (all)	2	0	
HICCUPS			
subjects affected / exposed	3 / 42 (7.14%)	1 / 22 (4.55%)	
occurrences (all)	3	1	
OROPHARYNGEAL PAIN			
subjects affected / exposed	4 / 42 (9.52%)	1 / 22 (4.55%)	
occurrences (all)	4	3	
PLEURAL EFFUSION			
subjects affected / exposed	1 / 42 (2.38%)	2 / 22 (9.09%)	
occurrences (all)	1	3	
PRODUCTIVE COUGH			
subjects affected / exposed	3 / 42 (7.14%)	1 / 22 (4.55%)	
occurrences (all)	3	2	
Psychiatric disorders			
AGITATION			
subjects affected / exposed	0 / 42 (0.00%)	1 / 22 (4.55%)	
occurrences (all)	0	1	
ANXIETY			
subjects affected / exposed	2 / 42 (4.76%)	2 / 22 (9.09%)	
occurrences (all)	2	2	
CONFUSIONAL STATE			
subjects affected / exposed	3 / 42 (7.14%)	1 / 22 (4.55%)	
occurrences (all)	5	1	
INSOMNIA			
subjects affected / exposed	4 / 42 (9.52%)	1 / 22 (4.55%)	
occurrences (all)	4	2	

Investigations			
WEIGHT DECREASED			
subjects affected / exposed	1 / 42 (2.38%)	1 / 22 (4.55%)	
occurrences (all)	1	1	
Injury, poisoning and procedural complications			
CONTUSION			
subjects affected / exposed	2 / 42 (4.76%)	2 / 22 (9.09%)	
occurrences (all)	2	2	
FALL			
subjects affected / exposed	1 / 42 (2.38%)	1 / 22 (4.55%)	
occurrences (all)	1	1	
LACERATION			
subjects affected / exposed	0 / 42 (0.00%)	2 / 22 (9.09%)	
occurrences (all)	0	2	
Cardiac disorders			
ATRIAL FIBRILLATION			
subjects affected / exposed	1 / 42 (2.38%)	1 / 22 (4.55%)	
occurrences (all)	1	1	
TACHYCARDIA			
subjects affected / exposed	2 / 42 (4.76%)	0 / 22 (0.00%)	
occurrences (all)	2	0	
Nervous system disorders			
DIZZINESS			
subjects affected / exposed	4 / 42 (9.52%)	1 / 22 (4.55%)	
occurrences (all)	4	1	
HEADACHE			
subjects affected / exposed	6 / 42 (14.29%)	3 / 22 (13.64%)	
occurrences (all)	6	6	
SCIATICA			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences (all)	0	0	
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	7 / 42 (16.67%)	4 / 22 (18.18%)	
occurrences (all)	17	25	
FEBRILE NEUTROPENIA			

subjects affected / exposed	12 / 42 (28.57%)	0 / 22 (0.00%)	
occurrences (all)	18	0	
LEUKOCYTOSIS			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences (all)	0	0	
LEUKOPENIA			
subjects affected / exposed	6 / 42 (14.29%)	1 / 22 (4.55%)	
occurrences (all)	21	1	
NEUTROPENIA			
subjects affected / exposed	14 / 42 (33.33%)	6 / 22 (27.27%)	
occurrences (all)	31	39	
THROMBOCYTOPENIA			
subjects affected / exposed	9 / 42 (21.43%)	6 / 22 (27.27%)	
occurrences (all)	41	23	
Gastrointestinal disorders			
ABDOMINAL DISTENSION			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences (all)	0	0	
ABDOMINAL PAIN			
subjects affected / exposed	7 / 42 (16.67%)	1 / 22 (4.55%)	
occurrences (all)	9	1	
ABDOMINAL PAIN UPPER			
subjects affected / exposed	6 / 42 (14.29%)	0 / 22 (0.00%)	
occurrences (all)	7	0	
CONSTIPATION			
subjects affected / exposed	16 / 42 (38.10%)	1 / 22 (4.55%)	
occurrences (all)	23	2	
DIARRHOEA			
subjects affected / exposed	21 / 42 (50.00%)	5 / 22 (22.73%)	
occurrences (all)	36	7	
DYSPEPSIA			
subjects affected / exposed	6 / 42 (14.29%)	0 / 22 (0.00%)	
occurrences (all)	6	0	
HAEMORRHOIDS			
subjects affected / exposed	4 / 42 (9.52%)	3 / 22 (13.64%)	
occurrences (all)	5	3	

MOUTH ULCERATION			
subjects affected / exposed	1 / 42 (2.38%)	0 / 22 (0.00%)	
occurrences (all)	1	0	
NAUSEA			
subjects affected / exposed	24 / 42 (57.14%)	3 / 22 (13.64%)	
occurrences (all)	34	3	
STOMATITIS			
subjects affected / exposed	4 / 42 (9.52%)	2 / 22 (9.09%)	
occurrences (all)	10	4	
VOMITING			
subjects affected / exposed	8 / 42 (19.05%)	3 / 22 (13.64%)	
occurrences (all)	9	5	
Skin and subcutaneous tissue disorders			
ERYTHEMA			
subjects affected / exposed	3 / 42 (7.14%)	0 / 22 (0.00%)	
occurrences (all)	3	0	
PETECHIAE			
subjects affected / exposed	1 / 42 (2.38%)	0 / 22 (0.00%)	
occurrences (all)	1	0	
PRURITUS			
subjects affected / exposed	6 / 42 (14.29%)	0 / 22 (0.00%)	
occurrences (all)	8	0	
RASH			
subjects affected / exposed	8 / 42 (19.05%)	1 / 22 (4.55%)	
occurrences (all)	12	1	
SKIN LESION			
subjects affected / exposed	0 / 42 (0.00%)	1 / 22 (4.55%)	
occurrences (all)	0	1	
SKIN ULCER			
subjects affected / exposed	1 / 42 (2.38%)	0 / 22 (0.00%)	
occurrences (all)	1	0	
Renal and urinary disorders			
HAEMATURIA			
subjects affected / exposed	1 / 42 (2.38%)	0 / 22 (0.00%)	
occurrences (all)	1	0	
RENAL FAILURE			

subjects affected / exposed	3 / 42 (7.14%)	0 / 22 (0.00%)	
occurrences (all)	3	0	
RENAL FAILURE ACUTE			
subjects affected / exposed	1 / 42 (2.38%)	0 / 22 (0.00%)	
occurrences (all)	1	0	
URINARY INCONTINENCE			
subjects affected / exposed	2 / 42 (4.76%)	1 / 22 (4.55%)	
occurrences (all)	2	1	
Musculoskeletal and connective tissue disorders			
ARTHRALGIA			
subjects affected / exposed	3 / 42 (7.14%)	2 / 22 (9.09%)	
occurrences (all)	3	2	
BACK PAIN			
subjects affected / exposed	2 / 42 (4.76%)	1 / 22 (4.55%)	
occurrences (all)	3	1	
BONE PAIN			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences (all)	0	0	
MUSCULOSKELETAL PAIN			
subjects affected / exposed	1 / 42 (2.38%)	2 / 22 (9.09%)	
occurrences (all)	1	2	
PAIN IN EXTREMITY			
subjects affected / exposed	2 / 42 (4.76%)	2 / 22 (9.09%)	
occurrences (all)	2	2	
Infections and infestations			
CELLULITIS			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences (all)	0	0	
LUNG INFECTION			
subjects affected / exposed	3 / 42 (7.14%)	0 / 22 (0.00%)	
occurrences (all)	7	0	
NASOPHARYNGITIS			
subjects affected / exposed	0 / 42 (0.00%)	2 / 22 (9.09%)	
occurrences (all)	0	5	
ORAL CANDIDIASIS			

subjects affected / exposed	3 / 42 (7.14%)	0 / 22 (0.00%)	
occurrences (all)	4	0	
ORAL HERPES			
subjects affected / exposed	6 / 42 (14.29%)	0 / 22 (0.00%)	
occurrences (all)	6	0	
PHARYNGITIS			
subjects affected / exposed	1 / 42 (2.38%)	2 / 22 (9.09%)	
occurrences (all)	1	2	
PNEUMONIA			
subjects affected / exposed	4 / 42 (9.52%)	4 / 22 (18.18%)	
occurrences (all)	4	5	
RESPIRATORY TRACT INFECTION			
subjects affected / exposed	0 / 42 (0.00%)	0 / 22 (0.00%)	
occurrences (all)	0	0	
SKIN INFECTION			
subjects affected / exposed	1 / 42 (2.38%)	2 / 22 (9.09%)	
occurrences (all)	1	2	
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	1 / 42 (2.38%)	1 / 22 (4.55%)	
occurrences (all)	2	1	
URINARY TRACT INFECTION			
subjects affected / exposed	0 / 42 (0.00%)	2 / 22 (9.09%)	
occurrences (all)	0	2	
Metabolism and nutrition disorders			
DECREASED APPETITE			
subjects affected / exposed	7 / 42 (16.67%)	2 / 22 (9.09%)	
occurrences (all)	11	4	
DEHYDRATION			
subjects affected / exposed	1 / 42 (2.38%)	0 / 22 (0.00%)	
occurrences (all)	1	0	
FLUID OVERLOAD			
subjects affected / exposed	3 / 42 (7.14%)	0 / 22 (0.00%)	
occurrences (all)	3	0	
FLUID RETENTION			

subjects affected / exposed	3 / 42 (7.14%)	0 / 22 (0.00%)	
occurrences (all)	4	0	
HYPOALBUMINAEMIA			
subjects affected / exposed	7 / 42 (16.67%)	1 / 22 (4.55%)	
occurrences (all)	10	1	
HYPOCALCAEMIA			
subjects affected / exposed	3 / 42 (7.14%)	1 / 22 (4.55%)	
occurrences (all)	4	1	
HYPOKALAEMIA			
subjects affected / exposed	16 / 42 (38.10%)	3 / 22 (13.64%)	
occurrences (all)	36	7	
HYPOMAGNESAEMIA			
subjects affected / exposed	6 / 42 (14.29%)	1 / 22 (4.55%)	
occurrences (all)	14	2	
HYPONATRAEMIA			
subjects affected / exposed	3 / 42 (7.14%)	1 / 22 (4.55%)	
occurrences (all)	5	1	
HYPOPHOSPHATAEMIA			
subjects affected / exposed	6 / 42 (14.29%)	1 / 22 (4.55%)	
occurrences (all)	13	2	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
10 February 2010	1. Modify the language around the countries where comparator products were designated as non-investigational product and to remove one of the comparator anthracyclines. At the time the original protocol was finalized, comparator product in the US, Canada, and Australia was to be commercially available product obtained through the local hospital pharmacy or licensed distributor and designated as non-investigational product (NIP). In all other countries, comparator product was to be supplied and packaged by Celgene Corporation and designated as investigational product (IP). With this amendment, the IP and NIP language were modified to allow comparator product to be designated as NIP in more countries than the original three countries (US, Canada, and Australia). 2. The original protocol allowed the investigator to choose one of three allowed anthracyclines (daunorubicin, idarubicin, or mitoxantrone) as part of the intensive chemotherapy comparator arm. Due to the infrequent use of mitoxantrone in the investigational sites, this amendment eliminated mitoxantrone as one of the anthracycline choices. 3. A new Celgene global multi-lingual call center for medical emergencies was opened. The global multilingual call center was to be used as a back-up when the Clinical Research Physician/Medical Monitor was not available for medical emergencies. The contact information for the call center was added to the protocol. 4. Other administrative textual changes and clarifications.
18 October 2010	1. Updated the format of the investigational new drug (IND) number. 2. Added an additional medical monitor contact. 3. Clarified the blinding of the central pathology reviewer. 4. Added clarification for the allowed visit window. 5. Clarified the BM aspirate/biopsy and peripheral blood smear collection times by treatment group. 6. Clarified that the collection of follow-up therapies was not required at End-of Study Visit. 7. Added language to accommodate the use of a BM aspirate and biopsy collected for disease diagnosis as part of the standard of care. 8. Clarified the BM aspirate and peripheral blood smear collection times following the last treatment cycle in the intensive chemotherapy arm. 9. Added dose modification guidelines for low-dose cytarabine. 10. Modified the administration language for low-dose cytarabine to allow the study sites more flexibility for home administration. 11. Added guidance for the use of prophylactic myeloid growth factor used in the intensive chemotherapy arm. 12. Increased the minimum ANC threshold for administration of prophylactic antibiotics. 13. Clarified that the EORTC QLQ-C30 instrument was to be performed using a portable electronic tablet computer. 14. Clarified pregnancy reporting requirements.

28 October 2011	1. Added sponsor name and address to protocol cover page. 2. Clarified the emergency contact was also the monitor. 3. Removed the requirement for PI title and site number from the PI and coordinating PI signature pages. 4. Allowed a ± 3 day window around the start of a cycle beginning at Cycle 2 and beyond. 5. Clarified requirements for stained and unstained peripheral blood smears. 6. Clarified the calculation of BSA was performed on Day 1 of each cycle and study drug dosing should have been calculated based on the BSA obtained on Day 1 of each cycle. 7. Clarified when a BM biopsy was to be collected. 8. Clarified the minimum allowable analyzable metaphases for those with a normal karyotype. 9. Clarified the volume for BM biomarker samples. 10. Clarified the use of hydroxyurea during the Screening Period. 11. Added AML with antecedent hematologic disorder such as chronic myelogenous leukemia or myeloproliferative neoplasms to excluded conditions. 12. Allowed the use of myeloid growth factor in those with previous episodes of neutropenic infection and at risk of subsequent neutropenic infection. 13. Clarified that the investigator could contact the medical monitor if guidance on azacitidine or low-dose cytarabine dose modification was needed. 14. Clarified the mCR definition. 15. Clarified the treatment failure indeterminate cause definition. 16. Clarified the progressive disease definition for peripheral blood. 17. Clarified the PR definition. 18. Clarified that, for AEs and SAEs, severity also means intensity. 19. Clarified the reporting requirements for duration and action taken for AEs and SAEs. 20. Clarified the reporting procedures for females who became pregnant and female partners of male study subjects who became pregnant. 21. Updated the name of the EMA. 22. Clarified the selection process for authorship of publications related to the study. 23. Added instructions that azacitidine was not to be filtered when preparing it for SC administration.
03 August 2012	The primary purpose of this Protocol Amendment was to remove the planned interim analysis. The original AZA-AML-001 study protocol called for an interim analysis for efficacy at approximately 60% (224 deaths) of the total expected deaths in the study. This number of deaths was anticipated to occur at approximately the same time as enrollment in the study was nearing completion. Following the Protocol Assistance with EMA, Celgene included the interim analysis to ensure that the sample size could be re-calculated and adapted during the enrollment phase of the study. Of note, there was no intention for the interim analysis to serve as a means to terminate the study for futility. As mentioned above, the timing of the interim was expected to occur at approximately the time when enrollment was estimated to be completed. However, due to a death rate lower than anticipated, the number of deaths required for the planned interim analysis was not reached before enrollment completion. Therefore, the interim analysis was thought to serve little purpose at this point in the study as part of the alpha level would have been wastefully spent before reaching the final analysis. 1. Updated the title of the contact person in section Medical Monitor / Emergency Contact Information. 2. Clarified the definition for EFS. 3. Clarified the definition for RFS. 4. Clarified the definition for the analysis of the duration of remission. 5. Clarified the population used for the patient-reported outcome analysis, ie, a modified ITT population and not the full ITT population.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported