



Clinical trial results:

A Phase 3, Multicenter, Open-label, Randomized Study of SGI-110 versus Treatment Choice (TC) in Adults with Previously Untreated Acute Myeloid Leukemia (AML) Who Are Not Considered Candidates for Intensive Remission Induction Chemotherapy

Summary

EudraCT number	2014-001233-89
Trial protocol	IT SE BE HU DE GB NL FI CZ AT ES PL FR DK
Global end of trial date	17 June 2019

Results information

Result version number	v1
This version publication date	29 June 2020
First version publication date	29 June 2020

Trial information

Trial identification

Sponsor protocol code	SGI-110-04
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02348489
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Astex Pharmaceuticals, Inc.
Sponsor organisation address	4420 Rosewood Drive, Suite 200, Pleasanton, United States, 94588
Public contact	Clinical trial info SGI-110-04, Astex Pharmaceuticals, Inc., SGI-110-04@astx.com
Scientific contact	Clinical trial info SGI-110-04, Astex Pharmaceuticals, Inc., SGI-110-04@astx.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	21 December 2018
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	17 June 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess and compare efficacy (complete response [CR] rate) and overall survival (OS) between SGI-110 and TC (treatment choice) in adults with previously untreated AML who are not considered candidates for intensive remission induction chemotherapy.

Protection of trial subjects:

The study was conducted in accordance with the International Conference on Harmonisation (ICH) Good Clinical Practice (GCP) guidelines, US Title 21 CFR Parts 11, 50, 54, 56, and 312, EU Clinical Trials Directive and its successor, local regulatory requirements, the principles enunciated in the Declaration of Helsinki, and all human clinical research regulations in countries where the study was conducted.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	19 March 2015
Long term follow-up planned	Yes
Long term follow-up rationale	Efficacy
Long term follow-up duration	4 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Netherlands: 2
Country: Number of subjects enrolled	Poland: 46
Country: Number of subjects enrolled	Romania: 4
Country: Number of subjects enrolled	Spain: 43
Country: Number of subjects enrolled	Sweden: 7
Country: Number of subjects enrolled	United Kingdom: 9
Country: Number of subjects enrolled	Austria: 11
Country: Number of subjects enrolled	Belgium: 19
Country: Number of subjects enrolled	Bulgaria: 14
Country: Number of subjects enrolled	Czech Republic: 34
Country: Number of subjects enrolled	Denmark: 8
Country: Number of subjects enrolled	Finland: 8
Country: Number of subjects enrolled	France: 99
Country: Number of subjects enrolled	Germany: 42
Country: Number of subjects enrolled	Hungary: 30
Country: Number of subjects enrolled	Italy: 88
Country: Number of subjects enrolled	Canada: 40

Country: Number of subjects enrolled	Australia: 27
Country: Number of subjects enrolled	Japan: 61
Country: Number of subjects enrolled	Russian Federation: 14
Country: Number of subjects enrolled	Serbia: 5
Country: Number of subjects enrolled	Korea, Republic of: 56
Country: Number of subjects enrolled	Taiwan: 23
Country: Number of subjects enrolled	United States: 125
Worldwide total number of subjects	815
EEA total number of subjects	464

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)	24
From 65 to 84 years	733
85 years and over	58

Subject disposition

Recruitment

Recruitment details:

The screening period was 19 March 2015 (first subject signed Informed Consent Form; ICF) to 25 November 2016 (last subject signed ICF), and the enrollment period was 23 March 2015 (first subject randomized) to 29 November 2016 (last subject randomized).

Pre-assignment

Screening details:

A total of 949 subjects were assessed for inclusion in the study. Of these, 134 subjects failed screening assessments and 815 subjects were randomized. Median follow-up was 766 days (25.5 months), with lower quartile follow-up of 671 days (22.4 months), and upper quartile follow-up of 896 days (29.9 months).

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	SGI-110 (Guadecitabine)

Arm description:

Guadecitabine 60 mg/m² was administered subcutaneously (SC) daily for 5 days (Days 1-5) in 28-day cycles.

Arm type	Experimental
Investigational medicinal product name	Guadecitabine
Investigational medicinal product code	
Other name	SGI-110
Pharmaceutical forms	Powder for concentrate for solution for injection/infusion
Routes of administration	Subcutaneous use

Dosage and administration details:

Guadecitabine 60 mg/m² was administered subcutaneously (SC) daily for 5 days (Days 1-5) in 28-day cycles.

Arm title	Treatment Choice
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Arm description:

One of the following treatment regimens was administered: 20 mg cytarabine subcutaneously (SC) twice daily (BID) on Days 1-10 every 28 days; 20 mg/m² decitabine given as a 1-hour intravenous (IV) infusion daily on Days 1-5 every 28 days; or 75 mg/m² azacitidine given IV or SC daily on Days 1-7 every 28 days.

Arm type	Experimental
Investigational medicinal product name	Cytarabine, decitabine, or azacitidine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and suspension for suspension for injection, Powder for concentrate for solution for injection/infusion
Routes of administration	Intravenous use, Subcutaneous use

Dosage and administration details:

One of the following treatment regimens was administered: 20 mg cytarabine subcutaneously (SC) twice daily (BID) on Days 1-10 every 28 days; 20 mg/m² decitabine given as a 1-hour intravenous (IV) infusion daily on Days 1-5 every 28 days; or 75 mg/m² azacitidine given IV or SC daily on Days 1-7 every 28 days.

Number of subjects in period 1	SGI-110 (Guadecitabine)	Treatment Choice
Started	408	407
Completed	28	28
Not completed	380	379
Consent withdrawn by subject	12	26
Death	331	331
Treatment ongoing at time of analysis	34	17
Lost to follow-up	3	5

Baseline characteristics

Reporting groups

Reporting group title	SGI-110 (Guadecitabine)
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Reporting group description:

Guadecitabine 60 mg/m² was administered subcutaneously (SC) daily for 5 days (Days 1-5) in 28-day cycles.

Reporting group title	Treatment Choice
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Reporting group description:

One of the following treatment regimens was administered: 20 mg cytarabine subcutaneously (SC) twice daily (BID) on Days 1-10 every 28 days; 20 mg/m² decitabine given as a 1-hour intravenous (IV) infusion daily on Days 1-5 every 28 days; or 75 mg/m² azacitidine given IV or SC daily on Days 1-7 every 28 days.

Reporting group values	SGI-110 (Guadecitabine)	Treatment Choice	Total
Number of subjects	408	407	815
Age categorical Units: Subjects			

Age continuous Units: years arithmetic mean standard deviation	75.9 ± 6.2	75.9 ± 5.8	-
Gender categorical Units: Subjects			
Female	177	165	342
Male	231	242	473

End points

End points reporting groups

Reporting group title	SGI-110 (Guadecitabine)
Reporting group description: Guadecitabine 60 mg/m ² was administered subcutaneously (SC) daily for 5 days (Days 1-5) in 28-day cycles.	
Reporting group title	Treatment Choice
Reporting group description: One of the following treatment regimens was administered: 20 mg cytarabine subcutaneously (SC) twice daily (BID) on Days 1-10 every 28 days; 20 mg/m ² decitabine given as a 1-hour intravenous (IV) infusion daily on Days 1-5 every 28 days; or 75 mg/m ² azacitidine given IV or SC daily on Days 1-7 every 28 days.	

Primary: Number of Subjects With a Complete Response (CR)

End point title	Number of Subjects With a Complete Response (CR)
End point description: Calculated as the number of subjects with a best response of CR divided by the total number of subjects included in the efficacy analysis. Response was assessed based on International Working Group 2003 acute myeloid leukemia (AML) response criteria by a blinded independent pathologist.	
End point type	Primary
End point timeframe: Median follow-up of 25.5 months	

End point values	SGI-110 (Guadecitabine)	Treatment Choice		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	408	407		
Units: Number				
Subjects	79	71		

Statistical analyses

Statistical analysis title	Difference in Complete Response
Statistical analysis description: The complete response rate was compared between the treatment groups using a Cochran Mantel-Haenszel (CMH) test at an alpha level of 0.04 stratified to adjust for stratification factors used at randomization: age (<75 or ≥ 75), Eastern Cooperative Oncology Group (ECOG) performance status (0-1, 2-3), study center region (North America, Europe, Rest of World), and secondary AML (secondary to MDS or other antecedent hematologic disorder) or poor-risk cytogenetics (Yes, No/Unknown).	
Comparison groups	SGI-110 (Guadecitabine) v Treatment Choice

Number of subjects included in analysis	815
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.482
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in response rate (%)
Point estimate	1.92
Confidence interval	
level	Other: 96 %
sides	2-sided
lower limit	-3.67
upper limit	7.5

Primary: Overall Survival

End point title	Overall Survival
End point description:	
Survival time was defined as the number of days from the day the subject was randomly assigned to study treatment to the date of death, regardless of cause, based on Kaplan-Meier estimates.	
End point type	Primary
End point timeframe:	
At 670 death events	

End point values	SGI-110 (Guadecitabine)	Treatment Choice		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	408	407		
Units: Days				
median (confidence interval 95%)	213 (187 to 255)	254 (223 to 282)		

Statistical analyses

Statistical analysis title	Overall Survival Comparison
Statistical analysis description:	
Overall survival curves were estimated using Kaplan-Meier method and compared between the treatment groups using a 2-sided stratification log-rank test, stratified by the same factors used at randomization: age (<75 or >= 75), Eastern Cooperative Oncology Group (ECOG) performance status (0-1, 2-3), study center region (North America, Europe, Rest of World), and secondary AML (secondary to MDS or other antecedent hematologic disorder) or poor-risk cytogenetics (Yes, No/Unknown).	
Comparison groups	SGI-110 (Guadecitabine) v Treatment Choice

Number of subjects included in analysis	815
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7328
Method	Stratified log-rank and Cox regression
Parameter estimate	Hazard ratio (HR)
Point estimate	0.97
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.83
upper limit	1.14

Secondary: Composite Complete Response Rate (CRc)

End point title	Composite Complete Response Rate (CRc)
End point description:	
CRc rate was calculated as the number of subjects with a best response of CR, complete response with incomplete platelet recovery (CRp), or complete response with incomplete blood count recovery (CRi) divided by the total number of subjects included in the efficacy analysis.	
End point type	Secondary
End point timeframe:	
Median follow-up of 25.5 months	

End point values	SGI-110 (Guadecitabine)	Treatment Choice		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	408	407		
Units: Percent				
number (not applicable)				
Percent	22.8	22.4		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Days Alive and Out of the Hospital (NDAOH)

End point title	Number of Days Alive and Out of the Hospital (NDAOH)
End point description:	
Duration of each hospital stay in days was calculated as the date of discharge minus date of admission. The Number of Days Alive and Out of the Hospital [up to 180 days] was calculated as: NDAOH = 180 - total duration of all hospital stays within 180 days from the first treatment - number of death days before Day 180. For subjects who were lost to follow-up within 6 months, the NDAOH was calculated conservatively assuming that the subject would have died the day after the last contact day.	
End point type	Secondary

End point timeframe:
Up to Month 6 (180 days)

End point values	SGI-110 (Guadecitabine)	Treatment Choice		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	408	407		
Units: Days				
arithmetic mean (standard deviation)	98.1 (± 63.60)	105.7 (± 63.58)		

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-free Survival (PFS)

End point title	Progression-free Survival (PFS)
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End point description:

Progression-free survival was defined as the number of days from randomization to the earliest date of investigator's assessment of disease progression, subject receiving an alternative anti-leukemia therapy (including haematopoietic cell transplant), or relapse by peripheral blood (PB) assessment or blinded bone marrow (BM) assessment, whichever occurred first, or death, regardless of cause, based on Kaplan-Meier estimates.

End point type	Secondary
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End point timeframe:

Median follow-up of 25.5 months

End point values	SGI-110 (Guadecitabine)	Treatment Choice		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	408	407		
Units: Days				
median (confidence interval 95%)	159 (136 to 178)	166 (148 to 179)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Red Blood Cell or Platelet Transfusions

End point title	Number of Red Blood Cell or Platelet Transfusions
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End point description:

The total number of red blood cells (RBCs) transfused or, separately, the total number of platelets transfused up to the 6-month time point for each subject was counted from the date of randomisation to Day 180, the date of last contact, or date of death, whichever occurred earlier. One RBC or platelet transfusion was defined as one unit, and a single bag of RBCs or platelets was considered one unit.

End point type	Secondary
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End point timeframe:

Up to Month 6

End point values	SGI-110 (Guadecitabine)	Treatment Choice		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	408	407		
Units: Transfusions				
arithmetic mean (standard deviation)				
Red blood cell transfusions	16.2 (± 11.84)	15.6 (± 13.02)		
Platelet transfusions	12.5 (± 18.78)	14.4 (± 39.10)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Health-related Quality of Life (QOL) Scores from Baseline: EQ-5D-5L

End point title	Change in Health-related Quality of Life (QOL) Scores from Baseline: EQ-5D-5L
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End point description:

EuroQol 5-level 5-dimension (EQ-5D-5L) descriptive scores were collected for each subject for a minimum of 6 months, unless the subject died or withdrew consent. Scores within each dimension for EQ-5D (mobility, self-care, usual activity, pain/discomfort, anxiety/depression) were calculated using counts and proportions. This study used the 5-level EQ-5D version, which consists of 5 levels of problems (where Level 1 is no problems and Level 5 indicates extreme problems).

End point type	Secondary
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End point timeframe:

At Month 6

End point values	SGI-110 (Guadecitabine)	Treatment Choice		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	408 ^[1]	407 ^[2]		
Units: Score on a scale				
arithmetic mean (standard deviation)				
Baseline	0.7767 (± 0.2160)	0.7663 (± 0.2291)		
Month 6	0.8252 (± 0.1825)	0.8240 (± 0.1948)		

Change from baseline	-0.0023 (\pm 0.1830)	0.0112 (\pm 0.2325)		
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Notes:

[1] - Baseline = 391 subjects; Month 6 = 180 subjects; Change from Baseline = 177 subjects

[2] - Baseline = 378 subjects; Month 6 = 183 subjects; Change from Baseline = 178 subjects

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Health-related Quality of Life (QOL) scores from baseline: EQ-VAS

End point title	Change in Health-related Quality of Life (QOL) scores from baseline: EQ-VAS
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End point description:

EuroQol-Visual Analogue Scale (EQ-VAS) descriptive scores were collected for each subject for a minimum of 6 months, unless the subject died or withdrew consent. A vertical 20-cm scale for EQ-VAS was used where the lowest value of 0 was labeled "the worst health you can imagine" and the top value of 100 was labeled "the best health you can imagine." Mean change in scores from baseline are summarised.

End point type	Secondary
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End point timeframe:

At Month 6

End point values	SGI-110 (Guadecitabine)	Treatment Choice		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	408 ^[3]	407 ^[4]		
Units: Score on a scale				
arithmetic mean (standard deviation)				
Baseline	64.64 (\pm 21.69)	63.58 (\pm 21.05)		
Month 6	72.76 (\pm 18.61)	71.72 (\pm 18.88)		
Change from baseline	3.28 (\pm 19.35)	3.67 (\pm 22.16)		

Notes:

[3] - Baseline = 391 subjects; Month 6 = 180 subjects; Change from Baseline = 177 subjects

[4] - Baseline = 377 subjects; Month 6 = 183 subjects; Change from Baseline = 178 subjects

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of CR

End point title	Duration of CR
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End point description:

Duration of CR (in number of days, based on Kaplan-Meier estimates) was calculated from the first time a CR was observed to the time of relapse, defined as the earliest time point whereby BM assessment or PB assessment indicated relapse/disease progression due to reappearance of leukemic blasts in PB or \geq 5% leukemic blasts in BM.

End point type	Secondary
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End point timeframe:

Median follow-up of 25.5 months

End point values	SGI-110 (Guadecitabine)	Treatment Choice		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	408	407		
Units: Days				
median (confidence interval 95%)	217 (175 to 261)	231 (182 to 289)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Median (range) duration of treatment was 5 cycles (1-38) for SGI-110 and 5 cycles (1-34) for Treatment Choice; safety data may be updated to include subjects still on treatment at the time of this analysis, pending CSR addendum.

Adverse event reporting additional description:

Treatment-emergent adverse events (TEAEs) were defined as events that first occurred or worsened after the first dose of study treatment given on Cycle 1 Day 1 until 30 days after the last dose of study treatment or the start of an alternative anti-leukemia treatment, whichever occurred first.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	21.0
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Reporting groups

Reporting group title	SGI-110 (Guadecitabine)
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Reporting group description:

Guadecitabine 60 mg/m² was administered subcutaneously (SC) daily for 5 days (Days 1-5) in 28-day cycles.

Reporting group title	Treatment Choice
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Reporting group description:

One of the following treatment regimens was administered: 20 mg cytarabine subcutaneously (SC) twice daily (BID) on Days 1-10 every 28 days; 20 mg/m² decitabine given as a 1-hour intravenous (IV) infusion daily on Days 1-5 every 28 days; or 75 mg/m² azacitidine given IV or SC daily on Days 1-7 every 28 days.

Serious adverse events	SGI-110 (Guadecitabine)	Treatment Choice	
Total subjects affected by serious adverse events			
subjects affected / exposed	325 / 401 (81.05%)	296 / 392 (75.51%)	
number of deaths (all causes)	329	331	
number of deaths resulting from adverse events	115	117	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
B-cell lymphoma			
subjects affected / exposed	0 / 401 (0.00%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Basal cell carcinoma			
subjects affected / exposed	2 / 401 (0.50%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bile duct cancer			

subjects affected / exposed	1 / 401 (0.25%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Biliary neoplasm			
subjects affected / exposed	1 / 401 (0.25%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Central nervous system leukaemia			
subjects affected / exposed	0 / 401 (0.00%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chloroma			
subjects affected / exposed	1 / 401 (0.25%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endometrial cancer metastatic			
subjects affected / exposed	1 / 401 (0.25%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Kaposi's sarcoma			
subjects affected / exposed	1 / 401 (0.25%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung adenocarcinoma			
subjects affected / exposed	1 / 401 (0.25%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Metastatic squamous cell carcinoma			
subjects affected / exposed	1 / 401 (0.25%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Squamous cell carcinoma			

subjects affected / exposed	1 / 401 (0.25%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transitional cell carcinoma			
subjects affected / exposed	1 / 401 (0.25%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tumour associated fever			
subjects affected / exposed	0 / 401 (0.00%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Aortic aneurysm			
subjects affected / exposed	0 / 401 (0.00%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic dissection			
subjects affected / exposed	1 / 401 (0.25%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Artery dissection			
subjects affected / exposed	1 / 401 (0.25%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Circulatory collapse			
subjects affected / exposed	5 / 401 (1.25%)	3 / 392 (0.77%)	
occurrences causally related to treatment / all	0 / 5	1 / 3	
deaths causally related to treatment / all	0 / 5	0 / 2	
Deep vein thrombosis			
subjects affected / exposed	2 / 401 (0.50%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematoma			

subjects affected / exposed	3 / 401 (0.75%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	1 / 3	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertension			
subjects affected / exposed	0 / 401 (0.00%)	2 / 392 (0.51%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypotension			
subjects affected / exposed	2 / 401 (0.50%)	3 / 392 (0.77%)	
occurrences causally related to treatment / all	1 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Iliac artery embolism			
subjects affected / exposed	0 / 401 (0.00%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Leriche syndrome			
subjects affected / exposed	1 / 401 (0.25%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Lupus vasculitis			
subjects affected / exposed	0 / 401 (0.00%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Orthostatic hypotension			
subjects affected / exposed	0 / 401 (0.00%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral arterial occlusive disease			
subjects affected / exposed	1 / 401 (0.25%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Phlebitis			

subjects affected / exposed	1 / 401 (0.25%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Shock			
subjects affected / exposed	1 / 401 (0.25%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Shock haemorrhagic			
subjects affected / exposed	0 / 401 (0.00%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Thrombophlebitis			
subjects affected / exposed	2 / 401 (0.50%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Venous thrombosis			
subjects affected / exposed	0 / 401 (0.00%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	4 / 401 (1.00%)	4 / 392 (1.02%)	
occurrences causally related to treatment / all	2 / 4	0 / 4	
deaths causally related to treatment / all	0 / 1	0 / 2	
Catheter site erythema			
subjects affected / exposed	1 / 401 (0.25%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest pain			
subjects affected / exposed	1 / 401 (0.25%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Death			

subjects affected / exposed	4 / 401 (1.00%)	5 / 392 (1.28%)	
occurrences causally related to treatment / all	0 / 4	0 / 5	
deaths causally related to treatment / all	0 / 4	0 / 5	
Device related thrombosis			
subjects affected / exposed	1 / 401 (0.25%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Discomfort			
subjects affected / exposed	0 / 401 (0.00%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fatigue			
subjects affected / exposed	1 / 401 (0.25%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gait disturbance			
subjects affected / exposed	0 / 401 (0.00%)	2 / 392 (0.51%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
General physical health deterioration			
subjects affected / exposed	7 / 401 (1.75%)	10 / 392 (2.55%)	
occurrences causally related to treatment / all	2 / 7	0 / 10	
deaths causally related to treatment / all	1 / 3	0 / 5	
Impaired healing			
subjects affected / exposed	0 / 401 (0.00%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injection site reaction			
subjects affected / exposed	1 / 401 (0.25%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malaise			

subjects affected / exposed	1 / 401 (0.25%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple organ dysfunction syndrome			
subjects affected / exposed	4 / 401 (1.00%)	4 / 392 (1.02%)	
occurrences causally related to treatment / all	0 / 4	0 / 4	
deaths causally related to treatment / all	0 / 2	0 / 3	
Non-cardiac chest pain			
subjects affected / exposed	2 / 401 (0.50%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oedema peripheral			
subjects affected / exposed	1 / 401 (0.25%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	15 / 401 (3.74%)	13 / 392 (3.32%)	
occurrences causally related to treatment / all	3 / 18	2 / 14	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sudden cardiac death			
subjects affected / exposed	0 / 401 (0.00%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Sudden death			
subjects affected / exposed	0 / 401 (0.00%)	2 / 392 (0.51%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 2	
Systemic inflammatory response syndrome			
subjects affected / exposed	1 / 401 (0.25%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	1 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Immune system disorders			
Anaphylactic reaction			

subjects affected / exposed	1 / 401 (0.25%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Acute pulmonary oedema			
subjects affected / exposed	2 / 401 (0.50%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute respiratory distress syndrome			
subjects affected / exposed	2 / 401 (0.50%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute respiratory failure			
subjects affected / exposed	2 / 401 (0.50%)	6 / 392 (1.53%)	
occurrences causally related to treatment / all	0 / 2	1 / 6	
deaths causally related to treatment / all	0 / 1	1 / 3	
Aspiration			
subjects affected / exposed	1 / 401 (0.25%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Asthma			
subjects affected / exposed	0 / 401 (0.00%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic obstructive pulmonary disease			
subjects affected / exposed	2 / 401 (0.50%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 3	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			
subjects affected / exposed	2 / 401 (0.50%)	2 / 392 (0.51%)	
occurrences causally related to treatment / all	1 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epistaxis			

subjects affected / exposed	3 / 401 (0.75%)	3 / 392 (0.77%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemoptysis			
subjects affected / exposed	0 / 401 (0.00%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Interstitial lung disease			
subjects affected / exposed	1 / 401 (0.25%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Laryngeal inflammation			
subjects affected / exposed	1 / 401 (0.25%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laryngeal oedema			
subjects affected / exposed	0 / 401 (0.00%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Organising pneumonia			
subjects affected / exposed	2 / 401 (0.50%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oropharyngeal pain			
subjects affected / exposed	1 / 401 (0.25%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			
subjects affected / exposed	6 / 401 (1.50%)	3 / 392 (0.77%)	
occurrences causally related to treatment / all	2 / 7	1 / 3	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pleuritic pain			

subjects affected / exposed	1 / 401 (0.25%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia aspiration			
subjects affected / exposed	1 / 401 (0.25%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonitis			
subjects affected / exposed	3 / 401 (0.75%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	1 / 3	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pulmonary alveolar haemorrhage			
subjects affected / exposed	0 / 401 (0.00%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pulmonary mass			
subjects affected / exposed	1 / 401 (0.25%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary oedema			
subjects affected / exposed	5 / 401 (1.25%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 5	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Respiratory distress			
subjects affected / exposed	2 / 401 (0.50%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	1 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Respiratory failure			
subjects affected / exposed	5 / 401 (1.25%)	2 / 392 (0.51%)	
occurrences causally related to treatment / all	0 / 5	0 / 2	
deaths causally related to treatment / all	0 / 3	0 / 1	
Stridor			

subjects affected / exposed	1 / 401 (0.25%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	2 / 401 (0.50%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary haemorrhage			
subjects affected / exposed	0 / 401 (0.00%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Psychiatric disorders			
Confusional state			
subjects affected / exposed	4 / 401 (1.00%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Delirium			
subjects affected / exposed	1 / 401 (0.25%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Depression			
subjects affected / exposed	0 / 401 (0.00%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Personality change			
subjects affected / exposed	0 / 401 (0.00%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suicide attempt			
subjects affected / exposed	1 / 401 (0.25%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Product issues			

Device dislocation			
subjects affected / exposed	0 / 401 (0.00%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Blood bilirubin increased			
subjects affected / exposed	1 / 401 (0.25%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
C-reactive protein increased			
subjects affected / exposed	2 / 401 (0.50%)	3 / 392 (0.77%)	
occurrences causally related to treatment / all	1 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza A virus test positive			
subjects affected / exposed	0 / 401 (0.00%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aspiration bronchial			
subjects affected / exposed	0 / 401 (0.00%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Allergic transfusion reaction			
subjects affected / exposed	1 / 401 (0.25%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ankle fracture			
subjects affected / exposed	1 / 401 (0.25%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Concussion			
subjects affected / exposed	0 / 401 (0.00%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Contusion			
subjects affected / exposed	0 / 401 (0.00%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Craniocerebral injury			
subjects affected / exposed	0 / 401 (0.00%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fall			
subjects affected / exposed	1 / 401 (0.25%)	2 / 392 (0.51%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femur fracture			
subjects affected / exposed	2 / 401 (0.50%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fibula fracture			
subjects affected / exposed	0 / 401 (0.00%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fracture			
subjects affected / exposed	1 / 401 (0.25%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemolytic transfusion reaction			
subjects affected / exposed	1 / 401 (0.25%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Head injury			
subjects affected / exposed	1 / 401 (0.25%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hip fracture			

subjects affected / exposed	1 / 401 (0.25%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Humerus fracture			
subjects affected / exposed	1 / 401 (0.25%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infusion related reaction			
subjects affected / exposed	1 / 401 (0.25%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pelvic fracture			
subjects affected / exposed	0 / 401 (0.00%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rib fracture			
subjects affected / exposed	0 / 401 (0.00%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal compression fracture			
subjects affected / exposed	1 / 401 (0.25%)	2 / 392 (0.51%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Splenic rupture			
subjects affected / exposed	0 / 401 (0.00%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subarachnoid haematoma			
subjects affected / exposed	1 / 401 (0.25%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subdural haematoma			

subjects affected / exposed	2 / 401 (0.50%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Subdural haemorrhage			
subjects affected / exposed	1 / 401 (0.25%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tibia fracture			
subjects affected / exposed	0 / 401 (0.00%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transfusion reaction			
subjects affected / exposed	4 / 401 (1.00%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Traumatic lung injury			
subjects affected / exposed	0 / 401 (0.00%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	1 / 1	
Cardiac disorders			
Acute coronary syndrome			
subjects affected / exposed	3 / 401 (0.75%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Acute myocardial infarction			
subjects affected / exposed	3 / 401 (0.75%)	3 / 392 (0.77%)	
occurrences causally related to treatment / all	0 / 6	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 1	
Angina pectoris			
subjects affected / exposed	3 / 401 (0.75%)	4 / 392 (1.02%)	
occurrences causally related to treatment / all	0 / 4	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arrhythmia			

subjects affected / exposed	1 / 401 (0.25%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			
subjects affected / exposed	5 / 401 (1.25%)	6 / 392 (1.53%)	
occurrences causally related to treatment / all	0 / 5	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial flutter			
subjects affected / exposed	1 / 401 (0.25%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial tachycardia			
subjects affected / exposed	1 / 401 (0.25%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrioventricular block complete			
subjects affected / exposed	0 / 401 (0.00%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac arrest			
subjects affected / exposed	3 / 401 (0.75%)	9 / 392 (2.30%)	
occurrences causally related to treatment / all	0 / 3	1 / 9	
deaths causally related to treatment / all	0 / 2	1 / 8	
Cardiac failure			
subjects affected / exposed	8 / 401 (2.00%)	10 / 392 (2.55%)	
occurrences causally related to treatment / all	0 / 8	0 / 11	
deaths causally related to treatment / all	0 / 5	0 / 3	
Cardiac failure acute			
subjects affected / exposed	1 / 401 (0.25%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cardiac failure chronic			

subjects affected / exposed	1 / 401 (0.25%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cardiac failure congestive			
subjects affected / exposed	4 / 401 (1.00%)	3 / 392 (0.77%)	
occurrences causally related to treatment / all	1 / 7	0 / 3	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cardiac tamponade			
subjects affected / exposed	0 / 401 (0.00%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardio-respiratory arrest			
subjects affected / exposed	1 / 401 (0.25%)	3 / 392 (0.77%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 1	0 / 3	
Cardiogenic shock			
subjects affected / exposed	1 / 401 (0.25%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiopulmonary failure			
subjects affected / exposed	2 / 401 (0.50%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 2	0 / 1	
Cardiorenal syndrome			
subjects affected / exposed	1 / 401 (0.25%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiovascular insufficiency			
subjects affected / exposed	1 / 401 (0.25%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Coronary artery stenosis			

subjects affected / exposed	1 / 401 (0.25%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			
subjects affected / exposed	1 / 401 (0.25%)	3 / 392 (0.77%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pericardial effusion			
subjects affected / exposed	0 / 401 (0.00%)	2 / 392 (0.51%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericarditis			
subjects affected / exposed	1 / 401 (0.25%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinus node dysfunction			
subjects affected / exposed	1 / 401 (0.25%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Supraventricular tachycardia			
subjects affected / exposed	1 / 401 (0.25%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Cerebral haemorrhage			
subjects affected / exposed	1 / 401 (0.25%)	2 / 392 (0.51%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 2	
Cerebrovascular accident			
subjects affected / exposed	6 / 401 (1.50%)	2 / 392 (0.51%)	
occurrences causally related to treatment / all	0 / 6	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 0	
Depressed level of consciousness			

subjects affected / exposed	0 / 401 (0.00%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Epilepsy			
subjects affected / exposed	0 / 401 (0.00%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Facial paralysis			
subjects affected / exposed	1 / 401 (0.25%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhage intracranial			
subjects affected / exposed	1 / 401 (0.25%)	4 / 392 (1.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 4	
Haemorrhagic stroke			
subjects affected / exposed	1 / 401 (0.25%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Headache			
subjects affected / exposed	1 / 401 (0.25%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intracranial haematoma			
subjects affected / exposed	0 / 401 (0.00%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic stroke			
subjects affected / exposed	2 / 401 (0.50%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Lethargy			

subjects affected / exposed	0 / 401 (0.00%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorder			
subjects affected / exposed	1 / 401 (0.25%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peroneal nerve palsy			
subjects affected / exposed	0 / 401 (0.00%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Presyncope			
subjects affected / exposed	0 / 401 (0.00%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seizure			
subjects affected / exposed	2 / 401 (0.50%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	1 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	2 / 401 (0.50%)	4 / 392 (1.02%)	
occurrences causally related to treatment / all	0 / 2	1 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient ischaemic attack			
subjects affected / exposed	1 / 401 (0.25%)	2 / 392 (0.51%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vocal cord paralysis			
subjects affected / exposed	0 / 401 (0.00%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Agranulocytosis			

subjects affected / exposed	1 / 401 (0.25%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anaemia			
subjects affected / exposed	16 / 401 (3.99%)	10 / 392 (2.55%)	
occurrences causally related to treatment / all	4 / 20	0 / 11	
deaths causally related to treatment / all	0 / 0	0 / 0	
Disseminated intravascular coagulation			
subjects affected / exposed	2 / 401 (0.50%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Febrile bone marrow aplasia			
subjects affected / exposed	3 / 401 (0.75%)	4 / 392 (1.02%)	
occurrences causally related to treatment / all	2 / 3	2 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile neutropenia			
subjects affected / exposed	101 / 401 (25.19%)	88 / 392 (22.45%)	
occurrences causally related to treatment / all	72 / 146	46 / 138	
deaths causally related to treatment / all	1 / 1	1 / 5	
Haemorrhagic diathesis			
subjects affected / exposed	2 / 401 (0.50%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	3 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Histiocytosis haematophagic			
subjects affected / exposed	1 / 401 (0.25%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Leukocytosis			
subjects affected / exposed	6 / 401 (1.50%)	2 / 392 (0.51%)	
occurrences causally related to treatment / all	0 / 7	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 0	
Lymphadenopathy			

subjects affected / exposed	1 / 401 (0.25%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphadenopathy mediastinal			
subjects affected / exposed	0 / 401 (0.00%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Monoclonal B-cell lymphocytosis			
subjects affected / exposed	1 / 401 (0.25%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenia			
subjects affected / exposed	2 / 401 (0.50%)	2 / 392 (0.51%)	
occurrences causally related to treatment / all	2 / 2	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancytopenia			
subjects affected / exposed	2 / 401 (0.50%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	2 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Splenic infarction			
subjects affected / exposed	0 / 401 (0.00%)	2 / 392 (0.51%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			
subjects affected / exposed	15 / 401 (3.74%)	5 / 392 (1.28%)	
occurrences causally related to treatment / all	7 / 15	1 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Mastoid disorder			
subjects affected / exposed	1 / 401 (0.25%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sudden hearing loss			

subjects affected / exposed	0 / 401 (0.00%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vertigo			
subjects affected / exposed	0 / 401 (0.00%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	4 / 401 (1.00%)	2 / 392 (0.51%)	
occurrences causally related to treatment / all	2 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain upper			
subjects affected / exposed	0 / 401 (0.00%)	2 / 392 (0.51%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal fissure			
subjects affected / exposed	1 / 401 (0.25%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal fistula			
subjects affected / exposed	1 / 401 (0.25%)	0 / 392 (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	3 / 401 (0.75%)	2 / 392 (0.51%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis ischaemic			
subjects affected / exposed	0 / 401 (0.00%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Constipation			

subjects affected / exposed	2 / 401 (0.50%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	7 / 401 (1.75%)	7 / 392 (1.79%)	
occurrences causally related to treatment / all	1 / 8	7 / 10	
deaths causally related to treatment / all	0 / 1	0 / 0	
Diverticular perforation			
subjects affected / exposed	0 / 401 (0.00%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulum			
subjects affected / exposed	0 / 401 (0.00%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspepsia			
subjects affected / exposed	0 / 401 (0.00%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysphagia			
subjects affected / exposed	1 / 401 (0.25%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enteritis			
subjects affected / exposed	1 / 401 (0.25%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Faecaloma			
subjects affected / exposed	0 / 401 (0.00%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric haemorrhage			

subjects affected / exposed	0 / 401 (0.00%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal haemorrhage			
subjects affected / exposed	2 / 401 (0.50%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhoids			
subjects affected / exposed	1 / 401 (0.25%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileus			
subjects affected / exposed	2 / 401 (0.50%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileus paralytic			
subjects affected / exposed	1 / 401 (0.25%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Incarcerated inguinal hernia			
subjects affected / exposed	0 / 401 (0.00%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal perforation			
subjects affected / exposed	0 / 401 (0.00%)	2 / 392 (0.51%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Intussusception			
subjects affected / exposed	0 / 401 (0.00%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Melaena			

subjects affected / exposed	3 / 401 (0.75%)	2 / 392 (0.51%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mesenteric artery thrombosis			
subjects affected / exposed	1 / 401 (0.25%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			
subjects affected / exposed	0 / 401 (0.00%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenic colitis			
subjects affected / exposed	1 / 401 (0.25%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophagitis			
subjects affected / exposed	1 / 401 (0.25%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis			
subjects affected / exposed	2 / 401 (0.50%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumatosis intestinalis			
subjects affected / exposed	1 / 401 (0.25%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Proctalgia			
subjects affected / exposed	0 / 401 (0.00%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal haemorrhage			

subjects affected / exposed	2 / 401 (0.50%)	4 / 392 (1.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal haemorrhage			
subjects affected / exposed	1 / 401 (0.25%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Stomatitis			
subjects affected / exposed	3 / 401 (0.75%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	2 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tooth disorder			
subjects affected / exposed	0 / 401 (0.00%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	1 / 401 (0.25%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	1 / 1	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal obstruction			
subjects affected / exposed	0 / 401 (0.00%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Biliary colic			
subjects affected / exposed	1 / 401 (0.25%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholangitis			
subjects affected / exposed	0 / 401 (0.00%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis acute			

subjects affected / exposed	1 / 401 (0.25%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gallbladder obstruction			
subjects affected / exposed	0 / 401 (0.00%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis acute			
subjects affected / exposed	1 / 401 (0.25%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic hepatitis			
subjects affected / exposed	1 / 401 (0.25%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Jaundice cholestatic			
subjects affected / exposed	1 / 401 (0.25%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Portal vein thrombosis			
subjects affected / exposed	0 / 401 (0.00%)	1 / 392 (0.26%)	
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			
Acute febrile neutrophilic dermatosis			
subjects affected / exposed	1 / 401 (0.25%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angioedema			
subjects affected / exposed	2 / 401 (0.50%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dermatitis			

subjects affected / exposed	0 / 401 (0.00%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eczema			
subjects affected / exposed	1 / 401 (0.25%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypersensitivity vasculitis			
subjects affected / exposed	1 / 401 (0.25%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyoderma gangrenosum			
subjects affected / exposed	1 / 401 (0.25%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	3 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rash generalised			
subjects affected / exposed	0 / 401 (0.00%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rash maculo-papular			
subjects affected / exposed	0 / 401 (0.00%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin disorder			
subjects affected / exposed	0 / 401 (0.00%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin ulcer			
subjects affected / exposed	0 / 401 (0.00%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Toxic skin eruption			

subjects affected / exposed	1 / 401 (0.25%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	11 / 401 (2.74%)	15 / 392 (3.83%)	
occurrences causally related to treatment / all	1 / 11	4 / 16	
deaths causally related to treatment / all	0 / 1	0 / 1	
Chronic kidney disease			
subjects affected / exposed	0 / 401 (0.00%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cystitis haemorrhagic			
subjects affected / exposed	1 / 401 (0.25%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematuria			
subjects affected / exposed	2 / 401 (0.50%)	2 / 392 (0.51%)	
occurrences causally related to treatment / all	0 / 2	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal colic			
subjects affected / exposed	0 / 401 (0.00%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal failure			
subjects affected / exposed	4 / 401 (1.00%)	2 / 392 (0.51%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ureterolithiasis			
subjects affected / exposed	0 / 401 (0.00%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary retention			

subjects affected / exposed	1 / 401 (0.25%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract obstruction			
subjects affected / exposed	1 / 401 (0.25%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Diabetes insipidus			
subjects affected / exposed	1 / 401 (0.25%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inappropriate antidiuretic hormone secretion			
subjects affected / exposed	1 / 401 (0.25%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Arthritis			
subjects affected / exposed	1 / 401 (0.25%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Back pain			
subjects affected / exposed	0 / 401 (0.00%)	2 / 392 (0.51%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bone pain			
subjects affected / exposed	2 / 401 (0.50%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bursitis			
subjects affected / exposed	1 / 401 (0.25%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Intervertebral disc protrusion			
subjects affected / exposed	0 / 401 (0.00%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Joint effusion			
subjects affected / exposed	0 / 401 (0.00%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lumbar spinal stenosis			
subjects affected / exposed	0 / 401 (0.00%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscle atrophy			
subjects affected / exposed	1 / 401 (0.25%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscle haemorrhage			
subjects affected / exposed	1 / 401 (0.25%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal pain			
subjects affected / exposed	0 / 401 (0.00%)	2 / 392 (0.51%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neck pain			
subjects affected / exposed	0 / 401 (0.00%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoarthritis			
subjects affected / exposed	2 / 401 (0.50%)	2 / 392 (0.51%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteonecrosis			

subjects affected / exposed	1 / 401 (0.25%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Pain in extremity			
subjects affected / exposed	1 / 401 (0.25%)	2 / 392 (0.51%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rhabdomyolysis			
subjects affected / exposed	1 / 401 (0.25%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal pain			
subjects affected / exposed	0 / 401 (0.00%)	2 / 392 (0.51%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Abdominal wall abscess			
subjects affected / exposed	1 / 401 (0.25%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abscess intestinal			
subjects affected / exposed	0 / 401 (0.00%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal abscess			
subjects affected / exposed	3 / 401 (0.75%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	1 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis			
subjects affected / exposed	1 / 401 (0.25%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthritis bacterial			

subjects affected / exposed	0 / 401 (0.00%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aspergillus infection			
subjects affected / exposed	3 / 401 (0.75%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	2 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atypical pneumonia			
subjects affected / exposed	0 / 401 (0.00%)	2 / 392 (0.51%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacteraemia			
subjects affected / exposed	7 / 401 (1.75%)	2 / 392 (0.51%)	
occurrences causally related to treatment / all	3 / 8	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacterial infection			
subjects affected / exposed	2 / 401 (0.50%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacteroides bacteraemia			
subjects affected / exposed	0 / 401 (0.00%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	5 / 401 (1.25%)	2 / 392 (0.51%)	
occurrences causally related to treatment / all	1 / 5	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchopulmonary aspergillosis			
subjects affected / exposed	2 / 401 (0.50%)	2 / 392 (0.51%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchopulmonary aspergillosis allergic			

subjects affected / exposed	0 / 401 (0.00%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Campylobacter gastroenteritis			
subjects affected / exposed	0 / 401 (0.00%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	3 / 401 (0.75%)	6 / 392 (1.53%)	
occurrences causally related to treatment / all	2 / 4	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis orbital			
subjects affected / exposed	1 / 401 (0.25%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cellulitis staphylococcal			
subjects affected / exposed	1 / 401 (0.25%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium colitis			
subjects affected / exposed	1 / 401 (0.25%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium difficile colitis			
subjects affected / exposed	4 / 401 (1.00%)	2 / 392 (0.51%)	
occurrences causally related to treatment / all	1 / 4	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium difficile infection			
subjects affected / exposed	4 / 401 (1.00%)	2 / 392 (0.51%)	
occurrences causally related to treatment / all	2 / 5	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cystitis			

subjects affected / exposed	3 / 401 (0.75%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dermo-hypodermatitis			
subjects affected / exposed	0 / 401 (0.00%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device related infection			
subjects affected / exposed	3 / 401 (0.75%)	7 / 392 (1.79%)	
occurrences causally related to treatment / all	0 / 3	2 / 8	
deaths causally related to treatment / all	0 / 0	1 / 1	
Device related sepsis			
subjects affected / exposed	2 / 401 (0.50%)	2 / 392 (0.51%)	
occurrences causally related to treatment / all	1 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulitis			
subjects affected / exposed	4 / 401 (1.00%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 6	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Encephalomyelitis			
subjects affected / exposed	1 / 401 (0.25%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocarditis			
subjects affected / exposed	0 / 401 (0.00%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterobacter infection			
subjects affected / exposed	1 / 401 (0.25%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epiglottitis			

subjects affected / exposed	1 / 401 (0.25%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Erysipelas			
subjects affected / exposed	2 / 401 (0.50%)	2 / 392 (0.51%)	
occurrences causally related to treatment / all	1 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia bacteraemia			
subjects affected / exposed	2 / 401 (0.50%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia infection			
subjects affected / exposed	1 / 401 (0.25%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia urinary tract infection			
subjects affected / exposed	2 / 401 (0.50%)	2 / 392 (0.51%)	
occurrences causally related to treatment / all	1 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye infection			
subjects affected / exposed	1 / 401 (0.25%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile infection			
subjects affected / exposed	1 / 401 (0.25%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric infection			
subjects affected / exposed	1 / 401 (0.25%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			

subjects affected / exposed	2 / 401 (0.50%)	2 / 392 (0.51%)	
occurrences causally related to treatment / all	1 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis viral			
subjects affected / exposed	1 / 401 (0.25%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gingivitis			
subjects affected / exposed	1 / 401 (0.25%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
H1N1 influenza			
subjects affected / exposed	0 / 401 (0.00%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematoma infection			
subjects affected / exposed	2 / 401 (0.50%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatosplenic abscess			
subjects affected / exposed	1 / 401 (0.25%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes simplex			
subjects affected / exposed	1 / 401 (0.25%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes zoster			
subjects affected / exposed	1 / 401 (0.25%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes zoster oticus			

subjects affected / exposed	1 / 401 (0.25%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infection			
subjects affected / exposed	6 / 401 (1.50%)	5 / 392 (1.28%)	
occurrences causally related to treatment / all	2 / 6	2 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infectious colitis			
subjects affected / exposed	0 / 401 (0.00%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			
subjects affected / exposed	6 / 401 (1.50%)	3 / 392 (0.77%)	
occurrences causally related to treatment / all	1 / 6	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injection site abscess			
subjects affected / exposed	1 / 401 (0.25%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injection site cellulitis			
subjects affected / exposed	1 / 401 (0.25%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injection site infection			
subjects affected / exposed	1 / 401 (0.25%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Kidney infection			
subjects affected / exposed	1 / 401 (0.25%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Klebsiella infection			

subjects affected / exposed	3 / 401 (0.75%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	1 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liver abscess			
subjects affected / exposed	1 / 401 (0.25%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Localised infection			
subjects affected / exposed	1 / 401 (0.25%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection			
subjects affected / exposed	0 / 401 (0.00%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mastoiditis			
subjects affected / exposed	1 / 401 (0.25%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mucormycosis			
subjects affected / exposed	1 / 401 (0.25%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	1 / 1	0 / 1	
Muscle abscess			
subjects affected / exposed	1 / 401 (0.25%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenic infection			
subjects affected / exposed	0 / 401 (0.00%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Osteomyelitis			

subjects affected / exposed	1 / 401 (0.25%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Otitis media			
subjects affected / exposed	0 / 401 (0.00%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Otitis media acute			
subjects affected / exposed	1 / 401 (0.25%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Parotitis			
subjects affected / exposed	2 / 401 (0.50%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pathogen resistance			
subjects affected / exposed	1 / 401 (0.25%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Periorbital cellulitis			
subjects affected / exposed	1 / 401 (0.25%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritonitis			
subjects affected / exposed	0 / 401 (0.00%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Periumbilical abscess			
subjects affected / exposed	1 / 401 (0.25%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pharyngitis			

subjects affected / exposed	2 / 401 (0.50%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 2	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumocystis jirovecii pneumonia			
subjects affected / exposed	0 / 401 (0.00%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pneumonia			
subjects affected / exposed	114 / 401 (28.43%)	77 / 392 (19.64%)	
occurrences causally related to treatment / all	40 / 143	24 / 100	
deaths causally related to treatment / all	4 / 20	3 / 22	
Pneumonia cytomegaloviral			
subjects affected / exposed	0 / 401 (0.00%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia influenzal			
subjects affected / exposed	0 / 401 (0.00%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia legionella			
subjects affected / exposed	1 / 401 (0.25%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural cellulitis			
subjects affected / exposed	0 / 401 (0.00%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative wound infection			
subjects affected / exposed	0 / 401 (0.00%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pseudomembranous colitis			

subjects affected / exposed	0 / 401 (0.00%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pseudomonal sepsis			
subjects affected / exposed	1 / 401 (0.25%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pseudomonas infection			
subjects affected / exposed	2 / 401 (0.50%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary tuberculosis			
subjects affected / exposed	1 / 401 (0.25%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulpitis dental			
subjects affected / exposed	0 / 401 (0.00%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis			
subjects affected / exposed	2 / 401 (0.50%)	2 / 392 (0.51%)	
occurrences causally related to treatment / all	1 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis acute			
subjects affected / exposed	1 / 401 (0.25%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal abscess			
subjects affected / exposed	0 / 401 (0.00%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory syncytial virus infection			

subjects affected / exposed	1 / 401 (0.25%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Scrotal infection			
subjects affected / exposed	1 / 401 (0.25%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	60 / 401 (14.96%)	44 / 392 (11.22%)	
occurrences causally related to treatment / all	17 / 81	14 / 55	
deaths causally related to treatment / all	4 / 26	4 / 20	
Septic shock			
subjects affected / exposed	16 / 401 (3.99%)	17 / 392 (4.34%)	
occurrences causally related to treatment / all	6 / 17	5 / 19	
deaths causally related to treatment / all	3 / 8	1 / 6	
Septic vasculitis			
subjects affected / exposed	1 / 401 (0.25%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinusitis			
subjects affected / exposed	0 / 401 (0.00%)	4 / 392 (1.02%)	
occurrences causally related to treatment / all	0 / 0	2 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinusitis fungal			
subjects affected / exposed	1 / 401 (0.25%)	0 / 392 (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	3 / 401 (0.75%)	2 / 392 (0.51%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal bacteraemia			

subjects affected / exposed	1 / 401 (0.25%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal infection			
subjects affected / exposed	1 / 401 (0.25%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal sepsis			
subjects affected / exposed	2 / 401 (0.50%)	3 / 392 (0.77%)	
occurrences causally related to treatment / all	0 / 2	1 / 3	
deaths causally related to treatment / all	0 / 1	0 / 0	
Streptococcal bacteraemia			
subjects affected / exposed	0 / 401 (0.00%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Systemic candida			
subjects affected / exposed	0 / 401 (0.00%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Systemic infection			
subjects affected / exposed	0 / 401 (0.00%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tonsillitis			
subjects affected / exposed	1 / 401 (0.25%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tooth infection			
subjects affected / exposed	2 / 401 (0.50%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	1 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tuberculosis pleurisy			

subjects affected / exposed	1 / 401 (0.25%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection			
subjects affected / exposed	4 / 401 (1.00%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	1 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urethritis			
subjects affected / exposed	1 / 401 (0.25%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	14 / 401 (3.49%)	10 / 392 (2.55%)	
occurrences causally related to treatment / all	2 / 16	2 / 11	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection enterococcal			
subjects affected / exposed	3 / 401 (0.75%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection staphylococcal			
subjects affected / exposed	1 / 401 (0.25%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urosepsis			
subjects affected / exposed	3 / 401 (0.75%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	1 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral infection			
subjects affected / exposed	1 / 401 (0.25%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound infection			

subjects affected / exposed	1 / 401 (0.25%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound infection staphylococcal			
subjects affected / exposed	2 / 401 (0.50%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis pseudomonas			
subjects affected / exposed	1 / 401 (0.25%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal skin infection			
subjects affected / exposed	1 / 401 (0.25%)	0 / 392 (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			
Decreased appetite			
subjects affected / exposed	2 / 401 (0.50%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dehydration			
subjects affected / exposed	2 / 401 (0.50%)	4 / 392 (1.02%)	
occurrences causally related to treatment / all	0 / 2	1 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Failure to thrive			
subjects affected / exposed	0 / 401 (0.00%)	1 / 392 (0.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypercalcaemia			
subjects affected / exposed	1 / 401 (0.25%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperglycaemia			

subjects affected / exposed	1 / 401 (0.25%)	2 / 392 (0.51%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoglycaemia			
subjects affected / exposed	1 / 401 (0.25%)	0 / 392 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypokalaemia			
subjects affected / exposed	2 / 401 (0.50%)	4 / 392 (1.02%)	
occurrences causally related to treatment / all	1 / 2	1 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyponatraemia			
subjects affected / exposed	1 / 401 (0.25%)	3 / 392 (0.77%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tumour lysis syndrome			
subjects affected / exposed	5 / 401 (1.25%)	2 / 392 (0.51%)	
occurrences causally related to treatment / all	1 / 5	2 / 2	
deaths causally related to treatment / all	0 / 2	0 / 0	

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

Non-serious adverse events	SGI-110 (Guadecitabine)	Treatment Choice	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	379 / 401 (94.51%)	371 / 392 (94.64%)	
Vascular disorders			
Haematoma			
subjects affected / exposed	25 / 401 (6.23%)	19 / 392 (4.85%)	
occurrences (all)	33	29	
Hypertension			
subjects affected / exposed	27 / 401 (6.73%)	25 / 392 (6.38%)	
occurrences (all)	40	37	
Hypotension			

subjects affected / exposed occurrences (all)	30 / 401 (7.48%) 39	31 / 392 (7.91%) 37	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	62 / 401 (15.46%)	56 / 392 (14.29%)	
occurrences (all)	104	82	
Fatigue			
subjects affected / exposed	63 / 401 (15.71%)	50 / 392 (12.76%)	
occurrences (all)	95	74	
Injection site reaction			
subjects affected / exposed	73 / 401 (18.20%)	48 / 392 (12.24%)	
occurrences (all)	148	75	
Oedema peripheral			
subjects affected / exposed	93 / 401 (23.19%)	78 / 392 (19.90%)	
occurrences (all)	123	108	
Pyrexia			
subjects affected / exposed	88 / 401 (21.95%)	110 / 392 (28.06%)	
occurrences (all)	153	174	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	79 / 401 (19.70%)	66 / 392 (16.84%)	
occurrences (all)	99	83	
Dyspnoea			
subjects affected / exposed	63 / 401 (15.71%)	51 / 392 (13.01%)	
occurrences (all)	82	60	
Epistaxis			
subjects affected / exposed	50 / 401 (12.47%)	36 / 392 (9.18%)	
occurrences (all)	67	51	
Oropharyngeal pain			
subjects affected / exposed	22 / 401 (5.49%)	23 / 392 (5.87%)	
occurrences (all)	29	27	
Pleural effusion			
subjects affected / exposed	21 / 401 (5.24%)	13 / 392 (3.32%)	
occurrences (all)	23	13	
Psychiatric disorders			

Anxiety subjects affected / exposed occurrences (all)	23 / 401 (5.74%) 23	22 / 392 (5.61%) 24	
Depression subjects affected / exposed occurrences (all)	14 / 401 (3.49%) 15	21 / 392 (5.36%) 21	
Insomnia subjects affected / exposed occurrences (all)	37 / 401 (9.23%) 50	45 / 392 (11.48%) 56	
Investigations Weight decreased subjects affected / exposed occurrences (all)	34 / 401 (8.48%) 46	25 / 392 (6.38%) 28	
Injury, poisoning and procedural complications Contusion subjects affected / exposed occurrences (all)	19 / 401 (4.74%) 22	22 / 392 (5.61%) 27	
Fall subjects affected / exposed occurrences (all)	33 / 401 (8.23%) 41	29 / 392 (7.40%) 37	
Nervous system disorders Dizziness subjects affected / exposed occurrences (all)	36 / 401 (8.98%) 47	42 / 392 (10.71%) 56	
Headache subjects affected / exposed occurrences (all)	30 / 401 (7.48%) 42	38 / 392 (9.69%) 53	
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all)	87 / 401 (21.70%) 197	78 / 392 (19.90%) 200	
Febrile neutropenia subjects affected / exposed occurrences (all)	66 / 401 (16.46%) 102	40 / 392 (10.20%) 57	
Leukopenia			

subjects affected / exposed	37 / 401 (9.23%)	33 / 392 (8.42%)	
occurrences (all)	119	124	
Neutropenia			
subjects affected / exposed	115 / 401 (28.68%)	88 / 392 (22.45%)	
occurrences (all)	309	230	
Thrombocytopenia			
subjects affected / exposed	116 / 401 (28.93%)	101 / 392 (25.77%)	
occurrences (all)	369	313	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	30 / 401 (7.48%)	46 / 392 (11.73%)	
occurrences (all)	43	50	
Abdominal pain upper			
subjects affected / exposed	21 / 401 (5.24%)	15 / 392 (3.83%)	
occurrences (all)	25	16	
Constipation			
subjects affected / exposed	124 / 401 (30.92%)	114 / 392 (29.08%)	
occurrences (all)	164	167	
Diarrhoea			
subjects affected / exposed	120 / 401 (29.93%)	83 / 392 (21.17%)	
occurrences (all)	164	116	
Haemorrhoids			
subjects affected / exposed	24 / 401 (5.99%)	19 / 392 (4.85%)	
occurrences (all)	28	24	
Nausea			
subjects affected / exposed	91 / 401 (22.69%)	107 / 392 (27.30%)	
occurrences (all)	141	149	
Stomatitis			
subjects affected / exposed	45 / 401 (11.22%)	38 / 392 (9.69%)	
occurrences (all)	56	44	
Vomiting			
subjects affected / exposed	56 / 401 (13.97%)	66 / 392 (16.84%)	
occurrences (all)	78	82	
Skin and subcutaneous tissue disorders			
Erythema			

subjects affected / exposed occurrences (all)	21 / 401 (5.24%) 21	17 / 392 (4.34%) 20	
Pruritus subjects affected / exposed occurrences (all)	22 / 401 (5.49%) 28	26 / 392 (6.63%) 32	
Rash subjects affected / exposed occurrences (all)	40 / 401 (9.98%) 51	28 / 392 (7.14%) 33	
Musculoskeletal and connective tissue disorders			
Arthralgia subjects affected / exposed occurrences (all)	24 / 401 (5.99%) 28	34 / 392 (8.67%) 38	
Back pain subjects affected / exposed occurrences (all)	34 / 401 (8.48%) 43	36 / 392 (9.18%) 43	
Pain in extremity subjects affected / exposed occurrences (all)	40 / 401 (9.98%) 51	32 / 392 (8.16%) 39	
Infections and infestations			
Bronchitis subjects affected / exposed occurrences (all)	22 / 401 (5.49%) 29	13 / 392 (3.32%) 15	
Cellulitis subjects affected / exposed occurrences (all)	29 / 401 (7.23%) 35	22 / 392 (5.61%) 25	
Nasopharyngitis subjects affected / exposed occurrences (all)	18 / 401 (4.49%) 27	20 / 392 (5.10%) 21	
Oral candidiasis subjects affected / exposed occurrences (all)	23 / 401 (5.74%) 27	17 / 392 (4.34%) 21	
Oral herpes subjects affected / exposed occurrences (all)	31 / 401 (7.73%) 36	20 / 392 (5.10%) 21	
Pneumonia			

subjects affected / exposed occurrences (all)	54 / 401 (13.47%) 64	30 / 392 (7.65%) 33	
Upper respiratory tract infection subjects affected / exposed occurrences (all)	21 / 401 (5.24%) 31	20 / 392 (5.10%) 28	
Urinary tract infection subjects affected / exposed occurrences (all)	33 / 401 (8.23%) 46	28 / 392 (7.14%) 39	
Metabolism and nutrition disorders			
Decreased appetite subjects affected / exposed occurrences (all)	89 / 401 (22.19%) 114	62 / 392 (15.82%) 80	
Hyperkalaemia subjects affected / exposed occurrences (all)	24 / 401 (5.99%) 33	13 / 392 (3.32%) 19	
Hypoalbuminaemia subjects affected / exposed occurrences (all)	26 / 401 (6.48%) 36	23 / 392 (5.87%) 43	
Hypocalcaemia subjects affected / exposed occurrences (all)	25 / 401 (6.23%) 30	18 / 392 (4.59%) 29	
Hypokalaemia subjects affected / exposed occurrences (all)	93 / 401 (23.19%) 170	77 / 392 (19.64%) 128	
Hypomagnesaemia subjects affected / exposed occurrences (all)	30 / 401 (7.48%) 49	27 / 392 (6.89%) 36	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
06 March 2015	Amendment 1 incorporates changes required by the Voluntary Harmonisation Procedure (VHP) assessment of the protocol after clinical trial application in Europe and sponsor administrative changes.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported