Clinical trial results:
A Randomized, Double-Blind, Multicenter Study of Denosumab Compared With Zoledronic Acid in the Treatment of Bone Disease in Subjects With Newly Diagnosed Multiple Myeloma

Summary

EudraCT number	2010-020454-34
Trial protocol	GR ES DE HU CZ GB PT IE IT AT BG SK LT
Global end of trial date	29 March 2019

Results information

Result version number	v1 (current)
This version publication date	04 April 2020
First version publication date	04 April 2020

Trial information

Trial identification

Sponsor protocol code	20090482

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01345019
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Amgen Inc.
Sponsor organisation address	One Amgen Center Drive, Thousand Oaks, CA, United States,
Public contact	IHQ Medical Info-Clinical Trials, Amgen (EUROPE) GmbH, MedInfoInternational@amgen.com
Scientific contact	IHQ Medical Info-Clinical Trials, Amgen (EUROPE) GmbH, MedInfoInternational@amgen.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	29 March 2019
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	29 March 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective was to determine if denosumab is noninferior to zoledronic acid with respect to the first on-study occurrence of an SRE in subjects with multiple myeloma.

Protection of trial subjects:

This study was conducted in accordance with International Conference on Harmonisation (ICH) Good Clinical Practice (GCP) regulations and guidelines, and Food and Drug Administration (FDA) regulations, and guidelines set forth in 21 CFR Parts 11, 50, 54, 56, and 312. All subjects provided written informed consent before undergoing any study-related procedures, including screening procedures. The study protocol, amendments, and the informed consent form (ICF) were reviewed by the Institutional Review Boards (IRBs) and Independent Ethics Committees (IECs). No subjects were recruited into the study and no investigational product (IP) was shipped until the IRB/IEC gave written approval of the protocol and ICF and Amgen received copies of these approvals.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	17 May 2012
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	France: 125
Country: Number of subjects enrolled	Russian Federation: 110
Country: Number of subjects enrolled	Greece: 94
Country: Number of subjects enrolled	Italy: 92
Country: Number of subjects enrolled	Bulgaria: 81
Country: Number of subjects enrolled	Poland: 77
Country: Number of subjects enrolled	Czech Republic: 75
Country: Number of subjects enrolled	Spain: 66
Country: Number of subjects enrolled	Ukraine: 60
Country: Number of subjects enrolled	Hungary: 47
Country: Number of subjects enrolled	Turkey: 42
Country: Number of subjects enrolled	United Kingdom: 33
Country: Number of subjects enrolled	Lithuania: 27
Country: Number of subjects enrolled	Austria: 26
Country: Number of subjects enrolled	Portugal: 25
Country: Number of subjects enrolled	Switzerland: 15
Country: Number of subjects enrolled	Ireland: 14

Country: Number of subjects enrolled	Slovakia: 7
Country: Number of subjects enrolled	Germany: 6
Country: Number of subjects enrolled	United States: 324
Country: Number of subjects enrolled	Canada: 121
Country: Number of subjects enrolled	Korea, Republic of: 84
Country: Number of subjects enrolled	Australia: 46
Country: Number of subjects enrolled	Japan: 42
Country: Number of subjects enrolled	Taiwan: 26
Country: Number of subjects enrolled	Singapore: 21
Country: Number of subjects enrolled	Malaysia: 14
Country: Number of subjects enrolled	Hong Kong: 9
Country: Number of subjects enrolled	New Zealand: 9
Worldwide total number of subjects	1718
EEA total number of subjects	795

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)	936
From 65 to 84 years	752
85 years and over	30

Subject disposition

Recruitment

Recruitment details:

This study was conducted at 259 centers across 29 countries in Europe, North America, Asia, Australia/New Zealand, and Japan. Participants were enrolled from 17 May 2012 to 29 March 2016.

Pre-assignment

Screening details:

Randomization was stratified according to: - intent to undergo autologous peripheral blood stem cell (PBSC) transplantation - the antimyeloma agent being utilized/planned to be utilized in first-line therapy - stage (International Staging System [ISS]) at diagnosis - previous SRE (yes or no) - region (Japan yes or no)

Period 1

Period 1 title	Blinded Treatment Phase
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor

Arms

Are arms mutually exclusive?	Yes
Arm title	Zoledronic Acid

Arm description:

Participants randomized to receive zoledronic acid 4 mg intravenously plus placebo to denosumab subcutaneously once every 4 weeks in the double-blind treatment phase.

Arm type	Active comparator
Investigational medicinal product name	zoledronic acid (active comparator)
Investigational medicinal product code	
Other name	Zometa®
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Administered by intravenous infusion over 15 minutes once every 4 weeks

Investigational medicinal product name	placebo to denosumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Administered by subcutaneous injection once every 4 weeks

Arm title	Denosumab

Arm description:

Participants randomized to receive denosumab 120 mg subcutaneously plus placebo to zoledronic acid intravenously once every 4 weeks in the double-blind treatment phase.

Arm type	Experimental
Investigational medicinal product name	denosumab (experimental)
Investigational medicinal product code	AMG 162
Other name	XGEVA®
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:	
Administered by subcutaneous injection once every 4 weeks	
Investigational medicinal product name	placebo to zoledronic acid
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Administered by intravenous infusion over 15 minutes once every 4 weeks

Number of subjects in period 1	Zoledronic Acid	Denosumab
Started	859	859
Received Treatment	852	850
Completed	541	555
Not completed	318	304
Consent withdrawn by subject	103	112
Ineligibility Determined	1	6
Adverse event, non-fatal	6	13
Protocol Deviation	5	-
Death	147	137
Completed Survival Follow-up	21	9
Administrative Decision	10	8
Lost to follow-up	6	3
Disease Progression	12	10
Noncompliance	5	3
Other, Not Specified	2	3

Period 2

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

Arms

Are arms mutually exclusive?	Yes

Arm title	Zoledronic Acid / Denosumab

Arm description:

Participants who randomized to receive zoledronic acid 4 mg intravenously plus placebo to denosumab subcutaneously (SC) once every 4 weeks (Q4W) in the double-blind treatment phase received denosumab 120 mg SC Q4W in the open-label treatment phase.

Arm type	Active comparator
Investigational medicinal product name	denosumab
Investigational medicinal product code	AMG 162
Other name	XGEVA®
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Administered by subcutaneous injection once every 4 weeks

Arm title	Denosumab / Denosumab

Arm description:

Participants who randomized to receive denosumab 120 mg subcutaneously (SC) plus placebo to zoledronic acid intravenouslyonce every 4 weeks (Q4W) in the double-blind treatment phase received denosumab 120 mg SC Q4W in the open-label treatment phase.

Arm type	Experimental
Investigational medicinal product name	denosumab
Investigational medicinal product code	AMG 162
Other name	XGEVA®
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Administered by subcutaneous injection once every 4 weeks

Number of subjects in period 2[1]	Zoledronic Acid / Denosumab	Denosumab / Denosumab
Started	418	426
Completed	227	233
Not completed	191	193
Consent withdrawn by subject	49	47
Adverse event, non-fatal	30	51
Death	49	48
Administrative Decision	30	15
Pregnancy	1	-
Lost to follow-up	1	2
Disease Progression	17	18
Noncompliance	5	4
Other, Not Specified	9	7
Protocol deviation	-	1

Notes:

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

Justification: Note for Period 1: Number of participants listed as "completed" in Period 1 were those participants still on-study as of the blinded treatment analysis cutoff date of 05 January 2017.
Note for Period 2: Participants who were still on study as of the blinded treatment analysis cutoff date but didn’t enter the open label treatment phase either entered a survival follow-up period or discontinued the study without the survival follow-up.

Baseline characteristics

Reporting groups	
Reporting group title	Zoledronic Acid
Reporting group description:	
Participants randomized to receive zoledronic acid 4 mg intravenously plus placebo to denosumab subcutaneously once every 4 weeks in the double-blind treatment phase.	
Reporting group title	Denosumab
Reporting group description:	
Participants randomized to receive denosumab 120 mg subcutaneously plus placebo to zoledronic acid intravenously once every 4 weeks in the double-blind treatment phase.	

Reporting group values	Zoledronic Acid	Denosumab	Total
Number of subjects	859	859	1718
Age Categorical Units: participants			
< 65 years	464	472	936
≥ 65 years	395	387	782
Age Continuous Units: years			
arithmetic mean	63.3	63.5	
standard deviation	± 10.5	± 10.6	-
Sex: Female, Male Units: participants			
Female	386	397	783
Male	473	462	935
Race/Ethnicity, Customized Units: Subjects			
White	699	711	1410
Asian	101	107	208
Black or African American	36	29	65
Other	19	10	29
American Indian or Alaska Native	3	0	3
Native Hawaiian or Other Pacific Islander	0	1	1
Multiracial	0	1	1
Missing	1	0	1
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	35	35	70
Not Hispanic or Latino	819	823	1642
Unknown or Not Reported	5	1	6
Eastern Cooperative Oncology Group (ECOG) Performance Status			
A scale to assess a patient's disease status. 0 = Fully active, able to carry out all pre-disease performance without restriction; 1 = Restricted in physically strenuous activity, ambulatory and able to carry out work of a light nature; 2 = Ambulatory and capable of all self-care, unable to carry out any work activities. Up and about > 50% of waking hours; 3 = Capable of only limited self-care, confined to bed or chair > 50% of waking hours; 4 = Completely disabled, confined to bed or chair; 5 = Dead.			
Units: Subjects			
0 (Fully active)	259	263	522

1 (Restricted but ambulatory)	413	400	813
2 (Ambulatory but unable to work)	187	196	383
Randomization Stratifications: Autologous Peripheral Blood Stem Cell (PBSC) Transplantation			
Randomization was stratified by - Intent to undergo autologous peripheral blood stem cell (PBSC) transplantation: yes or no.			
Units: Subjects			
Intent to undergo PBSC transplantation=Yes	465	465	930
Intent to undergo PBSC transplantation=No	394	394	788
Randomization Stratifications: Anti-Myeloma Agent Utilized/Planned in First-Line Therapy			
Randomization was stratified by: - The anti-myeloma agent being utilized/planned to be utilized in first-line therapy: novel therapy (included bortezomib, lenalidomide, or thalidomide) based or non-novel therapy-based.			
Units: Subjects			
Novel therapy	821	819	1640
Non-novel therapy	38	40	78
Randomization Stratifications: International Staging System (ISS) Stage at Diagnosis			
Randomization was stratified by - International Staging System (ISS) stage at diagnosis: I (serum β2 microglobulin < 3.5 mg/L; serum albumin ≥ 3.5 g/dL) or II (neither stage I or III) or III (serum β2 microglobulin ≥ 5.5 mg/L).			
Units: Subjects			
Stage I	268	263	531
Stage II	313	319	632
Stage III	278	277	555
Randomization Stratifications: Previous skeletal-related event (SRE)			
Randomization was stratified by - Previous skeletal-related event (SRE): yes or no.			
Units: Subjects			
Previous SRE=Yes	484	481	965
Previous SRE=No	375	378	753
Randomization Stratifications: Region (Japan, non-Japan)			
Randomization was stratified by - Region (Japan, non-Japan).			
Units: Subjects			
Japan	18	24	42
Non-Japan	841	835	1676

End points

End points reporting groups

Reporting group title	Zoledronic Acid
Reporting group description:	
Participants randomized to receive zoledronic acid 4 mg intravenously plus placebo to denosumab subcutaneously once every 4 weeks in the double-blind treatment phase.	
Reporting group title	Denosumab
Reporting group description:	
Participants randomized to receive denosumab 120 mg subcutaneously plus placebo to zoledronic acid intravenously once every 4 weeks in the double-blind treatment phase.	
Reporting group title	Zoledronic Acid / Denosumab
Reporting group description:	
Participants who randomized to receive zoledronic acid 4 mg intravenously plus placebo to denosumab subcutaneously (SC) once every 4 weeks (Q4W) in the double-blind treatment phase received denosumab 120 mg SC Q4W in the open-label treatment phase.	
Reporting group title	Denosumab / Denosumab
Reporting group description:	
Participants who randomized to receive denosumab 120 mg subcutaneously (SC) plus placebo to zoledronic acid intravenouslyonce every 4 weeks (Q4W) in the double-blind treatment phase received denosumab 120 mg SC Q4W in the open-label treatment phase.	

Primary: Time to First On-study Skeletal Related Event

End point title	Time to First On-study Skeletal Related Event
End point description:	
A skeletal-related event (SRE) is defined as one of the following: pathologic fracture (vertebral or non-vertebral), radiation therapy to bone (including the use of radioisotopes), surgery to bone, or spinal cord compression. Time to first on-study SRE is defined as the time interval (in days) from the randomization date to the date of first occurrence of on-study SRE. If there was no known event, and the participant was monitored for any one of the four SRE components, time to first on-study SRE was censored at the end of the treatment phase date or the primary analysis data cut-off date, whichever came first. 99999=Could not be estimated due to the low number of events.	
End point type	Primary
End point timeframe:	
From randomization until the primary analysis data cut-off date of 19 July 2016 (per protocol); median time on study was 17.6 and 17.3 months in each treatment group respectively.	

End point values	Zoledronic Acid	Denosumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	859	859		
Units: days				
median (confidence interval 95%)	730.0 (504.0 to 1014.0)	695.0 (448.0 to 99999)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Zoledronic Acid v Denosumab
Number of subjects included in analysis	1718
Analysis specification	Pre-specified
Analysis type	non-inferiority[1]
P-value	= 0.01 [2]
Method	Cox proportional hazards model
Parameter estimate	Hazard Ratio (< 1 favors denosumab)
Point estimate	0.98
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.85
upper limit	1.14

Notes:

[1] - A two-stage approach was used for the non-inferiority test. First, the fixed margin approach was used to ensure denosumab has an effect greater than placebo (ie, the non-inferiority margin M1, ie, the lower bound of the two-sided 95% confidence interval 1.28, is ruled out). Next, a synthesis method was used for the non-inferiority test of the hypothesis that denosumab preserved at least 50% of the effect of zoledronic acid (HR [95% CI] of 1.48 [1.28, 1.71] for placebo vs zoledronic acid.

[2] - Based on a Cox proportional hazards model stratified by the randomization stratification factors.

Primary: Percentage of Participants with an On-study Skeletal Related Event

End point title	Percentage of Participants with an On-study Skeletal Related Event[3]

End point description:

A skeletal-related event (SRE) is defined as one of the following: pathologic fracture (vertebral or non-vertebral), radiation therapy to bone (including the use of radioisotopes), surgery to bone, or spinal cord compression.

End point type	Primary

End point timeframe:

From randomization until the primary analysis data cut-off date of 19 July 2016 (per protocol); median time on study was 17.6 and 17.3 months in each treatment group respectively.

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Descriptive statistics are presented per protocol.

End point values	Zoledronic Acid	Denosumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	859	859		
Units: percentage of participants				
number (confidence interval 95%)	44.6 (41.3 to 47.9)	43.8 (40.5 to 47.1)		

Statistical analyses

No statistical analyses for this end point

Primary: Kaplan-Meier Estimate of Percentage of Participants with an On-study Skeletal Related Event

End point title	Kaplan-Meier Estimate of Percentage of Participants with an

	On-study Skeletal Related Event[4]

End point description:

A skeletal-related event (SRE) is defined as one of the following: pathologic fracture (vertebral or non-vertebral), radiation therapy to bone (including the use of radioisotopes), surgery to bone, or spinal cord compression.

End point type	Primary

End point timeframe:

From randomization until the primary analysis data cut-off date of 19 July 2016 (per protocol); median time on study was 17.6 and 17.3 months in each treatment group respectively. The Kaplan-Meier estimate at weeks 25, 49 and 109 is reported.

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Statistics for the Kaplan-Meier Estimate of Percentage of Participants With an On-study Skeletal Related Event are presented in the data table.

End point values	Zoledronic Acid	Denosumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	859	859		
Units: percentage of participants				
number (confidence interval 95%)				
At Week 25	36.5 (33.3 to 39.9)	35.9 (32.7 to 39.3)		
At Week 49	43.2 (39.7 to 46.8)	43.7 (40.2 to 47.3)		
At Week 109	50.6 (46.6 to 54.6)	50.5 (46.6 to 54.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to First On-study Skeletal Related Event - Superiority Analysis

End point title	Time to First On-study Skeletal Related Event - Superiority Analysis

End point description:

A skeletal-related event (SRE) is defined as one of the following: pathologic fracture (vertebral or non-vertebral), radiation therapy to bone (including the use of radioisotopes), surgery to bone, or spinal cord compression. Time to first on-study SRE is defined as the time interval (in days) from the randomization date to the date of first occurrence of on-study SRE. If there was no known event, and the participant was monitored for any one of the four SRE components, time to first on-study SRE was censored at the end of the treatment phase date or the primary analysis data cut-off date, whichever came first.
99999=Could not be estimated due to the low number of events.

End point type	Secondary

End point timeframe:

From randomization until the primary analysis data cut-off date of 19 July 2016 (per protocol); median time on study was 17.6 and 17.3 months in each treatment group respectively.

End point values	Zoledronic Acid	Denosumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	859	859		
Units: days				
median (confidence interval 95%)	730.0 (504.0 to 1014.0)	695.0 (448.0 to 99999)		

Statistical analyses

Statistical analysis title	Statisitcal Analysis 1
Comparison groups	Zoledronic Acid v Denosumab
Number of subjects included in analysis	1718
Analysis specification	Pre-specified
Analysis type	superiority[5]
P-value	= 0.82 [6]
Method	Logrank

Notes:

[5] - The statistical inferences of the treatment effect on secondary efficacy endpoints (time to the first on study SRE [superiority] and time to first and subsequent on study SRE [superiority, multiple event analysis]) were to be conducted if denosumab was determined to be non-inferior to zoledronic acid. To control the overall type I error for multiple comparisons at a significant level of 0.05, these secondary efficacy endpoints were tested simultaneously using the Hochberg procedure.

[6] - Based on a log rank test stratified by randomization stratification factors.

Secondary: Time to First and Subsequent On-Study Skeletal Related Event - Number of Events per Patient

End point title	Time to First and Subsequent On-Study Skeletal Related Event - Number of Events per Patient

End point description:

A skeletal-related event (SRE) is defined as one of the following: pathologic fracture (vertebral or non-vertebral), radiation therapy to bone (including the use of radioisotopes), surgery to bone, or spinal cord compression. Time to first on-study SRE is defined as the time interval (in days) from the randomization date to the date of first occurrence of on-study SRE. Time to a subsequent SRE is defined, similarly to the time to first on-study SRE, as the time interval from the randomization date to the date of a subsequent occurrence of on-study SRE, which had to be at least 21 days after the previous SRE.
A multiple event analysis was used, which accounts for both the absolute number of SREs and for the time between two consecutive events, and therefore, provides a more sensitive assessment of the risk of experiencing an SRE. The average number of events per patient is reported.

End point type	Secondary

End point timeframe:

From randomization until the primary analysis data cut-off date of 19 July 2016 (per protocol); median time on study was 17.6 and 17.3 months in each treatment group respectively.

End point values	Zoledronic Acid	Denosumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	859	859		
Units: events/patient				
number (not applicable)	0.66	0.66		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Zoledronic Acid v Denosumab
Number of subjects included in analysis	1718
Analysis specification	Pre-specified
Analysis type	superiority[7]
P-value	= 0.84 [8]
Method	Andersen-Gill model
Parameter estimate	Rate ratio (< 1 favors denosumab)
Point estimate	1.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.89
upper limit	1.15

Notes:

[7] - The statistical inferences of the treatment effect on secondary efficacy endpoints (time to the first on study SRE [superiority] and time to first and subsequent on study SRE [superiority, multiple event analysis]) were to be conducted if denosumab was determined to be non-inferior to zoledronic acid. To control the overall type I error for multiple comparisons at a significant level of 0.05, these secondary efficacy endpoints were tested simultaneously using the Hochberg procedure.
[8] - Based on an Andersen-Gill model stratified by the randomization stratification factors.

Secondary: Time to First and Subsequent On-Study Skeletal Related Event - Number of Events

End point title	Time to First and Subsequent On-Study Skeletal Related Event - Number of Events

End point description:

A skeletal-related event (SRE) is defined as one of the following: pathologic fracture (vertebral or non-vertebral), radiation therapy to bone (including the use of radioisotopes), surgery to bone, or spinal cord compression. Time to first on-study SRE is defined as the time interval (in days) from the randomization date to the date of first occurrence of on-study SRE. Time to a subsequent SRE is defined, similarly to the time to first on-study SRE, as the time interval from the randomization date to the date of a subsequent occurrence of on-study SRE, which had to be at least 21 days after the previous SRE.
A multiple event analysis was used, which accounts for both the absolute number of SREs and for the time between two consecutive events, and therefore, provides a more sensitive assessment of the risk of experiencing an SRE. The total number of events is reported.

End point type	Secondary

End point timeframe:

From randomization until the primary analysis data cut-off date of 19 July 2016 (per protocol); median time on study was 17.6 and 17.3 months in each treatment group respectively.

End point values	Zoledronic Acid	Denosumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	859	859		
Units: skeletal-related events	565	565		

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival

End point title	Overall Survival

End point description:

Overall survival was defined as the time interval (in days) from the randomization date to the date of death. If a participant was still alive at the primary analysis data cut-off date or was lost to follow-up by the primary analysis data cut-off date, survival time was censored at their last contact date or the primary analysis data cut-off date, whichever was first.
999999=Not estimable

End point type	Secondary

End point timeframe:

From randomization until the primary analysis data cut-off date of 19 July 2016 (per protocol); median time on study was 17.6 and 17.3 months in each treatment group respectively.

End point values	Zoledronic Acid	Denosumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	859	859		
Units: days				
median (confidence interval 95%)	999999 (-999999 to 999999)	1507.0 (-999999 to 999999)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

The survival function of time to death for each treatment group was estimated using Kaplan-Meier method and the hazard ratio of denosumab compared with zoledronic acid and its 2-sided 95% CI were estimated using a Cox proportional hazards model stratified by the randomization stratification factors and including treatment groups, age, race group, geographic region, baseline creatinine clearance, baseline risk per cytogenetic based prognosis, and baseline ECOG as independent variables.

Comparison groups	Zoledronic Acid v Denosumab

Number of subjects included in analysis	1718
Analysis specification	Pre-specified
Analysis type	superiority[9]
P-value	= 0.41
Method	Cox proportional hazards model
Parameter estimate	Hazard Ratio (< 1 favors denosumab)
Point estimate	0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.7
upper limit	1.16

Notes:

[9] - If superiority of denosumab over zoledronic acid was established for both time to first SRE and time to first and subsequent SRE, the additional secondary endpoint (overall survival) was to be tested at a significance level of 0.05.

Secondary: Percentage of Participants who Died

End point title	Percentage of Participants who Died

End point description:

End point type	Secondary

End point timeframe:

From randomization until the primary analysis data cut-off date of 19 July 2016 (per protocol); median time on study was 17.6 and 17.3 months in each treatment group respectively.

End point values	Zoledronic Acid	Denosumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	859	859		
Units: percentage of participants				
number (confidence interval 95%)	15.0 (12.6 to 17.4)	14.1 (11.8 to 16.4)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

DB: from 1st dose of study drug to the later of 30 days after last dose or end of treatment phase. OL: from 1st dose of OL study drug to end of study. Median months on study drug: 18.4 (ZA), 19.4 (Dmab) in DB; 23.2 (ZA/Dmab), 23.0 (Dmab/Dmab) in OL.

Adverse event reporting additional description:

The timeframe for deaths (all causes) is from the 1st dose of study drug to end of study. Participants who did not receive OL study drug but died in the survival follow-up phase are included in the DB columns. One participant who died before the 1st dose of study drug is excluded.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	22.0

Reporting groups

Reporting group title	DB: Zoledronic Acid

Reporting group description:

Participants received zoledronic acid 4 mg intravenously plus placebo to denosumab subcutaneously once every 4 weeks (Q4W) in the double-blind (DB) treatment phase.

Reporting group title	DB: Denosumab

Reporting group description:

Participants received denosumab 120 mg subcutaneously plus placebo to zoledronic acid intravenously once every 4 weeks (Q4W) in the double-blind (DB) treatment phase.

Reporting group title	OL: Zoledronic Acid / Denosumab

Reporting group description:

Participants who received zoledronic acid 4 mg intravenously plus placebo to denosumab subcutaneously (SC) once every 4 weeks (Q4W) in the double-blind treatment phase received denosumab 120 mg SC Q4W in the open-label (OL) treatment phase.

Reporting group title	OL: Denosumab / Denosumab

Reporting group description:

Participants who received denosumab 120 mg subcutaneously (SC) plus placebo to zoledronic acid intravenously once every 4 weeks (Q4W) in the double-blind treatment phase received denosumab 120 mg SC Q4W in the open-label (OL) treatment phase.

Serious adverse events	DB: Zoledronic Acid	DB: Denosumab	OL: Zoledronic Acid / Denosumab
Total subjects affected by serious adverse events			
subjects affected / exposed	447 / 852 (52.46%)	434 / 850 (51.06%)	159 / 418 (38.04%)
number of deaths (all causes)	169	154	49
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute myeloid leukaemia			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Adenocarcinoma of colon			

subjects affected / exposed	0 / 852 (0.00%)	2 / 850 (0.24%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Adenocarcinoma pancreas			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Basal cell carcinoma			
subjects affected / exposed	2 / 852 (0.23%)	1 / 850 (0.12%)	3 / 418 (0.72%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Basosquamous carcinoma of skin			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bladder cancer			
subjects affected / exposed	2 / 852 (0.23%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bladder cancer recurrent			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cervix carcinoma			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic myelomonocytic leukaemia			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colon cancer			

subjects affected / exposed	1 / 852 (0.12%)	3 / 850 (0.35%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 1	1 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colorectal cancer metastatic			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Diffuse large B-cell lymphoma			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endometrial adenocarcinoma			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatocellular carcinoma			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malignant melanoma			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malignant neoplasm of pleura			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malignant neoplasm of renal pelvis			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malignant pleural effusion			

subjects affected / exposed	1 / 852 (0.12%)	1 / 850 (0.12%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meningioma			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metastases to spine			
subjects affected / exposed	1 / 852 (0.12%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Neoplasm of orbit			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neuroendocrine tumour			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Non-Hodgkin's lymphoma			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Non-small cell lung cancer stage I			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Paraproteinaemia			
subjects affected / exposed	1 / 852 (0.12%)	3 / 850 (0.35%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 2	0 / 0
Plasma cell leukaemia			

subjects affected / exposed	4 / 852 (0.47%)	1 / 850 (0.12%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 5	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Plasma cell myeloma			
subjects affected / exposed	16 / 852 (1.88%)	18 / 850 (2.12%)	3 / 418 (0.72%)
occurrences causally related to treatment / all	0 / 19	0 / 21	0 / 3
deaths causally related to treatment / all	0 / 8	0 / 10	0 / 3
Plasma cell myeloma recurrent			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Plasmacytoma			
subjects affected / exposed	4 / 852 (0.47%)	7 / 850 (0.82%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 4	0 / 8	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 1
Prostate cancer			
subjects affected / exposed	2 / 852 (0.23%)	3 / 850 (0.35%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 2	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal adenocarcinoma			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sarcoma			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Squamous cell carcinoma of lung			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Squamous cell carcinoma of skin			

subjects affected / exposed	3 / 852 (0.35%)	0 / 850 (0.00%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute leukaemia			
subjects affected / exposed	0 / 852 (0.00%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute lymphocytic leukaemia			
subjects affected / exposed	0 / 852 (0.00%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute lymphocytic leukaemia recurrent			
subjects affected / exposed	0 / 852 (0.00%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Adenocarcinoma gastric			
subjects affected / exposed	0 / 852 (0.00%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anaplastic large-cell lymphoma			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bone marrow tumour cell infiltration			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Breast cancer			
subjects affected / exposed	0 / 852 (0.00%)	0 / 850 (0.00%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clear cell renal cell carcinoma			

subjects affected / exposed	0 / 852 (0.00%)	0 / 850 (0.00%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Glioblastoma multiforme			
subjects affected / exposed	0 / 852 (0.00%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intraductal proliferative breast lesion			
subjects affected / exposed	0 / 852 (0.00%)	0 / 850 (0.00%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung adenocarcinoma			
subjects affected / exposed	0 / 852 (0.00%)	0 / 850 (0.00%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malignant neoplasm progression			
subjects affected / exposed	0 / 852 (0.00%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metastases to bone			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Myelodysplastic syndrome			
subjects affected / exposed	0 / 852 (0.00%)	2 / 850 (0.24%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oropharyngeal cancer			
subjects affected / exposed	0 / 852 (0.00%)	0 / 850 (0.00%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prostate cancer metastatic			

subjects affected / exposed	0 / 852 (0.00%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal cord neoplasm			
subjects affected / exposed	0 / 852 (0.00%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Squamous cell carcinoma			
subjects affected / exposed	1 / 852 (0.12%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tumour pain			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Aortic aneurysm			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aortic aneurysm rupture			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Aortic dissection			
subjects affected / exposed	1 / 852 (0.12%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aortic dissection rupture			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Aortic thrombosis			

subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Circulatory collapse			
subjects affected / exposed	4 / 852 (0.47%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 4	0 / 1	0 / 0
Deep vein thrombosis			
subjects affected / exposed	8 / 852 (0.94%)	11 / 850 (1.29%)	2 / 418 (0.48%)
occurrences causally related to treatment / all	1 / 9	0 / 11	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Essential hypertension			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematoma			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertension			
subjects affected / exposed	0 / 852 (0.00%)	4 / 850 (0.47%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypotension			
subjects affected / exposed	1 / 852 (0.12%)	2 / 850 (0.24%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypovolaemic shock			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Orthostatic hypotension			

subjects affected / exposed	3 / 852 (0.35%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral arterial occlusive disease			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral artery aneurysm			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral ischaemia			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	2 / 418 (0.48%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Superior vena cava syndrome			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombophlebitis superficial			
subjects affected / exposed	1 / 852 (0.12%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombosis			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vasospasm			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aortic stenosis			

subjects affected / exposed	0 / 852 (0.00%)	0 / 850 (0.00%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arterial disorder			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertensive urgency			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Venous thrombosis			
subjects affected / exposed	0 / 852 (0.00%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Cataract operation			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fistula repair			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematopoietic stem cell mobilisation			
subjects affected / exposed	0 / 852 (0.00%)	2 / 850 (0.24%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Internal fixation of fracture			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intra-uterine contraceptive device removal			

subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Knee arthroplasty			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rehabilitation therapy			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Autologous haematopoietic stem cell transplant			
subjects affected / exposed	0 / 852 (0.00%)	2 / 850 (0.24%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	7 / 852 (0.82%)	3 / 850 (0.35%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 7	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chest pain			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chills			
subjects affected / exposed	1 / 852 (0.12%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Death			
subjects affected / exposed	3 / 852 (0.35%)	3 / 850 (0.35%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 3	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 3	0 / 3	0 / 1
Disease progression			

subjects affected / exposed	1 / 852 (0.12%)	2 / 850 (0.24%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Fatigue			
subjects affected / exposed	1 / 852 (0.12%)	1 / 850 (0.12%)	2 / 418 (0.48%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gait disturbance			
subjects affected / exposed	1 / 852 (0.12%)	2 / 850 (0.24%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General physical health deterioration			
subjects affected / exposed	10 / 852 (1.17%)	10 / 850 (1.18%)	2 / 418 (0.48%)
occurrences causally related to treatment / all	0 / 11	0 / 15	0 / 3
deaths causally related to treatment / all	0 / 2	0 / 6	0 / 1
Generalised oedema			
subjects affected / exposed	0 / 852 (0.00%)	3 / 850 (0.35%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperpyrexia			
subjects affected / exposed	1 / 852 (0.12%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Hyperthermia			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Localised oedema			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malaise			

subjects affected / exposed	0 / 852 (0.00%)	2 / 850 (0.24%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mucosal ulceration			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Multiple organ dysfunction syndrome			
subjects affected / exposed	6 / 852 (0.70%)	5 / 850 (0.59%)	3 / 418 (0.72%)
occurrences causally related to treatment / all	0 / 6	0 / 6	0 / 4
deaths causally related to treatment / all	0 / 6	0 / 5	0 / 3
Non-cardiac chest pain			
subjects affected / exposed	5 / 852 (0.59%)	4 / 850 (0.47%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 5	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oedema peripheral			
subjects affected / exposed	3 / 852 (0.35%)	5 / 850 (0.59%)	2 / 418 (0.48%)
occurrences causally related to treatment / all	0 / 3	1 / 5	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Performance status decreased			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	28 / 852 (3.29%)	24 / 850 (2.82%)	2 / 418 (0.48%)
occurrences causally related to treatment / all	5 / 32	0 / 37	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Sudden cardiac death			
subjects affected / exposed	1 / 852 (0.12%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 1	0 / 0
Sudden death			

subjects affected / exposed	5 / 852 (0.59%)	3 / 850 (0.35%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 5	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 5	0 / 3	0 / 1
Oedema			
subjects affected / exposed	0 / 852 (0.00%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Systemic inflammatory response syndrome			
subjects affected / exposed	0 / 852 (0.00%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Acute graft versus host disease			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute graft versus host disease in intestine			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anaphylactic reaction			
subjects affected / exposed	1 / 852 (0.12%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypersensitivity			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Serum sickness			
subjects affected / exposed	0 / 852 (0.00%)	0 / 850 (0.00%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast			

disorders			
Adenomyosis			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Benign prostatic hyperplasia			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Scrotal oedema			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Testicular mass			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Acute pulmonary oedema			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Acute respiratory distress syndrome			
subjects affected / exposed	2 / 852 (0.23%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute respiratory failure			
subjects affected / exposed	2 / 852 (0.23%)	2 / 850 (0.24%)	2 / 418 (0.48%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspiration			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Asthma			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchial obstruction			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchopneumopathy			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic obstructive pulmonary disease			
subjects affected / exposed	4 / 852 (0.47%)	4 / 850 (0.47%)	3 / 418 (0.72%)
occurrences causally related to treatment / all	0 / 8	0 / 5	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cough			
subjects affected / exposed	0 / 852 (0.00%)	3 / 850 (0.35%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	10 / 852 (1.17%)	5 / 850 (0.59%)	2 / 418 (0.48%)
occurrences causally related to treatment / all	0 / 10	0 / 5	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epistaxis			
subjects affected / exposed	1 / 852 (0.12%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoxia			
subjects affected / exposed	3 / 852 (0.35%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	1 / 3	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Interstitial lung disease			

subjects affected / exposed	3 / 852 (0.35%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	1 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung disorder			
subjects affected / exposed	2 / 852 (0.23%)	3 / 850 (0.35%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 2	0 / 4	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nasal discomfort			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Non-cardiogenic pulmonary oedema			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Pleural effusion			
subjects affected / exposed	4 / 852 (0.47%)	6 / 850 (0.71%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 4	0 / 9	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Pneumonia aspiration			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonitis			
subjects affected / exposed	0 / 852 (0.00%)	6 / 850 (0.71%)	2 / 418 (0.48%)
occurrences causally related to treatment / all	0 / 0	0 / 6	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumothorax			
subjects affected / exposed	2 / 852 (0.23%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Productive cough			

subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary artery thrombosis			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Pulmonary embolism			
subjects affected / exposed	13 / 852 (1.53%)	16 / 850 (1.88%)	5 / 418 (1.20%)
occurrences causally related to treatment / all	0 / 13	0 / 16	0 / 5
deaths causally related to treatment / all	0 / 2	0 / 2	0 / 1
Pulmonary fibrosis			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary oedema			
subjects affected / exposed	2 / 852 (0.23%)	2 / 850 (0.24%)	2 / 418 (0.48%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 2
Respiratory acidosis			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory distress			
subjects affected / exposed	1 / 852 (0.12%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure			
subjects affected / exposed	11 / 852 (1.29%)	4 / 850 (0.47%)	4 / 418 (0.96%)
occurrences causally related to treatment / all	0 / 12	0 / 4	0 / 4
deaths causally related to treatment / all	0 / 4	0 / 1	0 / 2
Stridor			

subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Asphyxia			
subjects affected / exposed	0 / 852 (0.00%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchiectasis			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea exertional			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural disorder			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural thickening			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleuritic pain			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary haemorrhage			
subjects affected / exposed	0 / 852 (0.00%)	0 / 850 (0.00%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary hypertension			

subjects affected / exposed	0 / 852 (0.00%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 852 (0.12%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Completed suicide			
subjects affected / exposed	2 / 852 (0.23%)	0 / 850 (0.00%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 2	0 / 0	0 / 1
Confusional state			
subjects affected / exposed	3 / 852 (0.35%)	5 / 850 (0.59%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 6	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Delirium			
subjects affected / exposed	2 / 852 (0.23%)	4 / 850 (0.47%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 5	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Depression			
subjects affected / exposed	0 / 852 (0.00%)	3 / 850 (0.35%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Disorientation			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Major depression			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mental status changes			

subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mutism			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychotic disorder			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicide attempt			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Adjustment disorder			
subjects affected / exposed	0 / 852 (0.00%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Drug dependence			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Organic brain syndrome			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric decompensation			
subjects affected / exposed	0 / 852 (0.00%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Product issues			
Device breakage			

subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device failure			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device occlusion			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device dislocation			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Acute hepatic failure			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Bile duct stenosis			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholangitis acute			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis			
subjects affected / exposed	0 / 852 (0.00%)	2 / 850 (0.24%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis acute			

subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholelithiasis			
subjects affected / exposed	2 / 852 (0.23%)	0 / 850 (0.00%)	2 / 418 (0.48%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Drug-induced liver injury			
subjects affected / exposed	1 / 852 (0.12%)	2 / 850 (0.24%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic function abnormal			
subjects affected / exposed	0 / 852 (0.00%)	2 / 850 (0.24%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 5	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatitis toxic			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperbilirubinaemia			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bile duct obstruction			
subjects affected / exposed	0 / 852 (0.00%)	0 / 850 (0.00%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis chronic			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gallbladder rupture			

subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic failure			
subjects affected / exposed	0 / 852 (0.00%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatitis			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatotoxicity			
subjects affected / exposed	0 / 852 (0.00%)	0 / 850 (0.00%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Jaundice cholestatic			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 852 (0.00%)	3 / 850 (0.35%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 852 (0.00%)	3 / 850 (0.35%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bilirubin conjugated increased			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood bilirubin increased			

subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood creatine increased			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood creatinine increased			
subjects affected / exposed	3 / 852 (0.35%)	2 / 850 (0.24%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	1 / 3	2 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood electrolytes abnormal			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood immunoglobulin G increased			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Blood immunoglobulin M increased			
subjects affected / exposed	2 / 852 (0.23%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood lactate dehydrogenase increased			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Body temperature increased			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bone marrow plasmacyte count increased			

subjects affected / exposed	2 / 852 (0.23%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
C-reactive protein increased			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chest X-ray abnormal			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eastern Cooperative Oncology Group performance status worsened			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemoglobin decreased			
subjects affected / exposed	1 / 852 (0.12%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Heart rate irregular			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Light chain analysis increased			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Liver function test abnormal			
subjects affected / exposed	1 / 852 (0.12%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Monoclonal immunoglobulin present			

subjects affected / exposed	1 / 852 (0.12%)	2 / 850 (0.24%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Neutrophil count decreased			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Platelet count decreased			
subjects affected / exposed	6 / 852 (0.70%)	2 / 850 (0.24%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 8	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Weight decreased			
subjects affected / exposed	1 / 852 (0.12%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
White blood cell count decreased			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood immunoglobulin A increased			
subjects affected / exposed	1 / 852 (0.12%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Influenza A virus test positive			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Light chain analysis abnormal			
subjects affected / exposed	0 / 852 (0.00%)	0 / 850 (0.00%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Plasma cells increased			

subjects affected / exposed	0 / 852 (0.00%)	0 / 850 (0.00%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Plasma cells present			
subjects affected / exposed	0 / 852 (0.00%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Protein urine present			
subjects affected / exposed	0 / 852 (0.00%)	0 / 850 (0.00%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
White blood cell count increased			
subjects affected / exposed	0 / 852 (0.00%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Abdominal injury			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Anastomotic leak			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bone contusion			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Brain contusion			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Cervical vertebral fracture			

subjects affected / exposed	0 / 852 (0.00%)	2 / 850 (0.24%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Concussion			
subjects affected / exposed	0 / 852 (0.00%)	2 / 850 (0.24%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Fall			
subjects affected / exposed	6 / 852 (0.70%)	3 / 850 (0.35%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 6	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femoral neck fracture			
subjects affected / exposed	7 / 852 (0.82%)	2 / 850 (0.24%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 7	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femur fracture			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fibula fracture			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hand fracture			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Head injury			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hip fracture			

subjects affected / exposed	2 / 852 (0.23%)	3 / 850 (0.35%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 3	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Humerus fracture			
subjects affected / exposed	2 / 852 (0.23%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Joint dislocation			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lumbar vertebral fracture			
subjects affected / exposed	8 / 852 (0.94%)	4 / 850 (0.47%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 8	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Patella fracture			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural haemorrhage			
subjects affected / exposed	2 / 852 (0.23%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Procedural pain			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rib fracture			
subjects affected / exposed	2 / 852 (0.23%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal compression fracture			

subjects affected / exposed	0 / 852 (0.00%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal fracture			
subjects affected / exposed	0 / 852 (0.00%)	0 / 850 (0.00%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sternal fracture			
subjects affected / exposed	0 / 852 (0.00%)	2 / 850 (0.24%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subdural haematoma			
subjects affected / exposed	1 / 852 (0.12%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Tendon rupture			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thoracic vertebral fracture			
subjects affected / exposed	5 / 852 (0.59%)	6 / 850 (0.71%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 5	0 / 7	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tibia fracture			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transfusion related complication			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ankle fracture			

subjects affected / exposed	0 / 852 (0.00%)	0 / 850 (0.00%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Compression fracture			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Craniocerebral injury			
subjects affected / exposed	0 / 852 (0.00%)	0 / 850 (0.00%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Facial bones fracture			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Incarcerated incisional hernia			
subjects affected / exposed	0 / 852 (0.00%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infusion related reaction			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury			
subjects affected / exposed	0 / 852 (0.00%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Limb fracture			
subjects affected / exposed	0 / 852 (0.00%)	0 / 850 (0.00%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Poisoning			

subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 1
Post procedural fever			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Procedural nausea			
subjects affected / exposed	0 / 852 (0.00%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary contusion			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin laceration			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound dehiscence			
subjects affected / exposed	0 / 852 (0.00%)	0 / 850 (0.00%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Congenital, familial and genetic disorders			
Aplasia			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Odontogenic cyst			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			

Acute coronary syndrome			
subjects affected / exposed	1 / 852 (0.12%)	2 / 850 (0.24%)	3 / 418 (0.72%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute myocardial infarction			
subjects affected / exposed	6 / 852 (0.70%)	2 / 850 (0.24%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 7	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 5	0 / 0	0 / 0
Angina pectoris			
subjects affected / exposed	2 / 852 (0.23%)	2 / 850 (0.24%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina unstable			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	2 / 418 (0.48%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial fibrillation			
subjects affected / exposed	10 / 852 (1.17%)	4 / 850 (0.47%)	2 / 418 (0.48%)
occurrences causally related to treatment / all	0 / 12	0 / 5	0 / 3
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Atrial flutter			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial tachycardia			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bradycardia			
subjects affected / exposed	4 / 852 (0.47%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 5	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac amyloidosis			

subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac arrest			
subjects affected / exposed	11 / 852 (1.29%)	6 / 850 (0.71%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 12	0 / 6	0 / 1
deaths causally related to treatment / all	0 / 11	0 / 5	0 / 1
Cardiac disorder			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure			
subjects affected / exposed	7 / 852 (0.82%)	11 / 850 (1.29%)	3 / 418 (0.72%)
occurrences causally related to treatment / all	0 / 8	0 / 13	0 / 3
deaths causally related to treatment / all	0 / 1	0 / 6	0 / 2
Cardiac failure acute			
subjects affected / exposed	2 / 852 (0.23%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 2	0 / 1	0 / 0
Cardiac failure chronic			
subjects affected / exposed	0 / 852 (0.00%)	3 / 850 (0.35%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 5	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 1
Cardiac failure congestive			
subjects affected / exposed	5 / 852 (0.59%)	5 / 850 (0.59%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 5	0 / 6	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Cardio-respiratory arrest			
subjects affected / exposed	2 / 852 (0.23%)	0 / 850 (0.00%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 2	0 / 0	0 / 1
Cardiopulmonary failure			

subjects affected / exposed	2 / 852 (0.23%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Cardiovascular insufficiency			
subjects affected / exposed	1 / 852 (0.12%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 0
Coronary artery disease			
subjects affected / exposed	1 / 852 (0.12%)	2 / 850 (0.24%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 2	0 / 0
Left ventricular failure			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mitral valve stenosis			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	2 / 852 (0.23%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial ischaemia			
subjects affected / exposed	1 / 852 (0.12%)	2 / 850 (0.24%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Myocarditis			
subjects affected / exposed	1 / 852 (0.12%)	2 / 850 (0.24%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Palpitations			

subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pericarditis			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinus bradycardia			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinus node dysfunction			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinus tachycardia			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Supraventricular tachycardia			
subjects affected / exposed	2 / 852 (0.23%)	3 / 850 (0.35%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tachyarrhythmia			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tachycardia			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tricuspid valve incompetence			

subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute left ventricular failure			
subjects affected / exposed	0 / 852 (0.00%)	0 / 850 (0.00%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Arrhythmia			
subjects affected / exposed	0 / 852 (0.00%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac tamponade			
subjects affected / exposed	0 / 852 (0.00%)	0 / 850 (0.00%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac valve disease			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiomyopathy			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Left ventricular dysfunction			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pericardial effusion			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ventricular arrhythmia			

subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Basilar migraine			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Brain injury			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cauda equina syndrome			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral haemorrhage			
subjects affected / exposed	4 / 852 (0.47%)	0 / 850 (0.00%)	2 / 418 (0.48%)
occurrences causally related to treatment / all	0 / 4	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 2	0 / 0	0 / 1
Cerebral ischaemia			
subjects affected / exposed	3 / 852 (0.35%)	2 / 850 (0.24%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 3	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral vasoconstriction			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrovascular accident			
subjects affected / exposed	5 / 852 (0.59%)	5 / 850 (0.59%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 5	0 / 6	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Cognitive disorder			

subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coma			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Depressed level of consciousness			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dizziness			
subjects affected / exposed	4 / 852 (0.47%)	2 / 850 (0.24%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	1 / 4	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Encephalopathy			
subjects affected / exposed	3 / 852 (0.35%)	2 / 850 (0.24%)	2 / 418 (0.48%)
occurrences causally related to treatment / all	0 / 3	0 / 3	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Epilepsy			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Generalised tonic-clonic seizure			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhage intracranial			
subjects affected / exposed	3 / 852 (0.35%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhagic stroke			

subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hemiparesis			
subjects affected / exposed	1 / 852 (0.12%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hemiplegia			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoaesthesia			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic cerebral infarction			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic stroke			
subjects affected / exposed	1 / 852 (0.12%)	3 / 850 (0.35%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Lacunar infarction			
subjects affected / exposed	0 / 852 (0.00%)	2 / 850 (0.24%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Loss of consciousness			
subjects affected / exposed	2 / 852 (0.23%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lumbosacral radiculopathy			

subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nerve degeneration			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neuropathy peripheral			
subjects affected / exposed	1 / 852 (0.12%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Paralysis			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Paraparesis			
subjects affected / exposed	2 / 852 (0.23%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Paraplegia			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Paresis			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Polyneuropathy			
subjects affected / exposed	1 / 852 (0.12%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Presyncope			

subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Radiculopathy			
subjects affected / exposed	2 / 852 (0.23%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sciatica			
subjects affected / exposed	2 / 852 (0.23%)	2 / 850 (0.24%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seizure			
subjects affected / exposed	1 / 852 (0.12%)	3 / 850 (0.35%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seizure like phenomena			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal cord compression			
subjects affected / exposed	8 / 852 (0.94%)	4 / 850 (0.47%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 8	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subarachnoid haemorrhage			
subjects affected / exposed	1 / 852 (0.12%)	1 / 850 (0.12%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	9 / 852 (1.06%)	7 / 850 (0.82%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 10	0 / 7	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient ischaemic attack			

subjects affected / exposed	1 / 852 (0.12%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Brain oedema			
subjects affected / exposed	0 / 852 (0.00%)	0 / 850 (0.00%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral atrophy			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral haematoma			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral infarction			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrovascular disorder			
subjects affected / exposed	0 / 852 (0.00%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cervical cord compression			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dementia			
subjects affected / exposed	0 / 852 (0.00%)	0 / 850 (0.00%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Encephalitis post varicella			

subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Headache			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intracranial mass			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Myelopathy			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Parkinson's disease			
subjects affected / exposed	0 / 852 (0.00%)	0 / 850 (0.00%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Agranulocytosis			
subjects affected / exposed	1 / 852 (0.12%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anaemia			
subjects affected / exposed	26 / 852 (3.05%)	12 / 850 (1.41%)	5 / 418 (1.20%)
occurrences causally related to treatment / all	1 / 33	0 / 17	0 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Autoimmune haemolytic anaemia			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bicytopenia			

subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bone marrow failure			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile neutropenia			
subjects affected / exposed	25 / 852 (2.93%)	23 / 850 (2.71%)	7 / 418 (1.67%)
occurrences causally related to treatment / all	0 / 29	0 / 25	0 / 9
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Haemolytic anaemia			
subjects affected / exposed	1 / 852 (0.12%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperviscosity syndrome			
subjects affected / exposed	0 / 852 (0.00%)	3 / 850 (0.35%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 2	0 / 0
Leukocytosis			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Leukopenia			
subjects affected / exposed	2 / 852 (0.23%)	2 / 850 (0.24%)	2 / 418 (0.48%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenia			
subjects affected / exposed	13 / 852 (1.53%)	4 / 850 (0.47%)	4 / 418 (0.96%)
occurrences causally related to treatment / all	0 / 16	0 / 4	0 / 7
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancytopenia			

subjects affected / exposed	4 / 852 (0.47%)	2 / 850 (0.24%)	3 / 418 (0.72%)
occurrences causally related to treatment / all	0 / 4	0 / 2	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 2
Thrombocytopenia			
subjects affected / exposed	12 / 852 (1.41%)	9 / 850 (1.06%)	2 / 418 (0.48%)
occurrences causally related to treatment / all	0 / 15	0 / 9	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acquired haemophilia with anti FVIII, XI, or XIII			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anaemia of malignant disease			
subjects affected / exposed	0 / 852 (0.00%)	0 / 850 (0.00%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cytopenia			
subjects affected / exposed	0 / 852 (0.00%)	0 / 850 (0.00%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Platelet disorder			
subjects affected / exposed	0 / 852 (0.00%)	0 / 850 (0.00%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytosis			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	1 / 852 (0.12%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vertigo positional			

subjects affected / exposed	1 / 852 (0.12%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Cataract			
subjects affected / exposed	2 / 852 (0.23%)	0 / 850 (0.00%)	2 / 418 (0.48%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diplopia			
subjects affected / exposed	1 / 852 (0.12%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Exophthalmos			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Extraocular muscle paresis			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ulcerative keratitis			
subjects affected / exposed	0 / 852 (0.00%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vision blurred			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal distension			

subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal hernia			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal incarcerated hernia			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain			
subjects affected / exposed	5 / 852 (0.59%)	1 / 850 (0.12%)	4 / 418 (0.96%)
occurrences causally related to treatment / all	0 / 5	0 / 1	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain lower			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain upper			
subjects affected / exposed	2 / 852 (0.23%)	2 / 850 (0.24%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal wall haematoma			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic gastritis			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis			

subjects affected / exposed	1 / 852 (0.12%)	2 / 850 (0.24%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis ischaemic			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Constipation			
subjects affected / exposed	4 / 852 (0.47%)	3 / 850 (0.35%)	2 / 418 (0.48%)
occurrences causally related to treatment / all	0 / 4	0 / 3	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	10 / 852 (1.17%)	9 / 850 (1.06%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 11	0 / 10	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea haemorrhagic			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulum intestinal			
subjects affected / exposed	0 / 852 (0.00%)	2 / 850 (0.24%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Duodenal ulcer			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Duodenal ulcer haemorrhage			
subjects affected / exposed	1 / 852 (0.12%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dysphagia			

subjects affected / exposed	1 / 852 (0.12%)	3 / 850 (0.35%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enteritis			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastritis			
subjects affected / exposed	1 / 852 (0.12%)	2 / 850 (0.24%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastritis erosive			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal amyloidosis			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal haemorrhage			
subjects affected / exposed	5 / 852 (0.59%)	3 / 850 (0.35%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 7	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 2	0 / 0	0 / 0
Gastrointestinal perforation			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 1
Gingivitis ulcerative			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hiatus hernia			

subjects affected / exposed	0 / 852 (0.00%)	2 / 850 (0.24%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ileus			
subjects affected / exposed	0 / 852 (0.00%)	0 / 850 (0.00%)	2 / 418 (0.48%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Inguinal hernia			
subjects affected / exposed	2 / 852 (0.23%)	2 / 850 (0.24%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal haemorrhage			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal obstruction			
subjects affected / exposed	3 / 852 (0.35%)	1 / 850 (0.12%)	2 / 418 (0.48%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestinal obstruction			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestine perforation			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestine polyp			
subjects affected / exposed	1 / 852 (0.12%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower gastrointestinal haemorrhage			

subjects affected / exposed	2 / 852 (0.23%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mechanical ileus			
subjects affected / exposed	0 / 852 (0.00%)	2 / 850 (0.24%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Melaena			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mouth haemorrhage			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	4 / 852 (0.47%)	4 / 850 (0.47%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 4	0 / 4	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophagitis			
subjects affected / exposed	2 / 852 (0.23%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Proctitis			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal haemorrhage			

subjects affected / exposed	2 / 852 (0.23%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal obstruction			
subjects affected / exposed	0 / 852 (0.00%)	4 / 850 (0.47%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 5	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 1
Stomatitis			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subileus			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Umbilical hernia			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	11 / 852 (1.29%)	7 / 850 (0.82%)	3 / 418 (0.72%)
occurrences causally related to treatment / all	0 / 14	0 / 7	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anal fissure			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendiceal mucocoele			
subjects affected / exposed	0 / 852 (0.00%)	0 / 850 (0.00%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Crohn's disease			

subjects affected / exposed	0 / 852 (0.00%)	0 / 850 (0.00%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspepsia			
subjects affected / exposed	0 / 852 (0.00%)	0 / 850 (0.00%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric ulcer haemorrhage			
subjects affected / exposed	0 / 852 (0.00%)	0 / 850 (0.00%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal pain			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 852 (0.00%)	0 / 850 (0.00%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gingival bleeding			
subjects affected / exposed	0 / 852 (0.00%)	0 / 850 (0.00%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal ischaemia			
subjects affected / exposed	0 / 852 (0.00%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Jejunal perforation			
subjects affected / exposed	0 / 852 (0.00%)	0 / 850 (0.00%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestinal haemorrhage			

subjects affected / exposed	0 / 852 (0.00%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Obstructive pancreatitis			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Retroperitoneal mass			
subjects affected / exposed	0 / 852 (0.00%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal perforation			
subjects affected / exposed	0 / 852 (0.00%)	0 / 850 (0.00%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Toothache			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper gastrointestinal haemorrhage			
subjects affected / exposed	0 / 852 (0.00%)	0 / 850 (0.00%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Drug eruption			
subjects affected / exposed	2 / 852 (0.23%)	0 / 850 (0.00%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	1 / 2	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Erythema multiforme			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperhidrosis			

subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Keloid scar			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Purpura			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rash			
subjects affected / exposed	0 / 852 (0.00%)	2 / 850 (0.24%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rash macular			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rash maculo-papular			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin disorder			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urticaria			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angioedema			

subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Decubitus ulcer			
subjects affected / exposed	2 / 852 (0.23%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rash generalised			
subjects affected / exposed	0 / 852 (0.00%)	0 / 850 (0.00%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin ulcer			
subjects affected / exposed	0 / 852 (0.00%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	24 / 852 (2.82%)	17 / 850 (2.00%)	8 / 418 (1.91%)
occurrences causally related to treatment / all	5 / 27	2 / 18	0 / 9
deaths causally related to treatment / all	0 / 2	0 / 0	0 / 2
Bladder perforation			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic kidney disease			
subjects affected / exposed	1 / 852 (0.12%)	2 / 850 (0.24%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cystitis haemorrhagic			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dysuria			

subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematuria			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nephrolithiasis			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal colic			
subjects affected / exposed	0 / 852 (0.00%)	2 / 850 (0.24%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal disorder			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal failure			
subjects affected / exposed	7 / 852 (0.82%)	4 / 850 (0.47%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 8	0 / 4	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal impairment			
subjects affected / exposed	1 / 852 (0.12%)	2 / 850 (0.24%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ureteric obstruction			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ureterolithiasis			

subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary retention			
subjects affected / exposed	2 / 852 (0.23%)	2 / 850 (0.24%)	2 / 418 (0.48%)
occurrences causally related to treatment / all	0 / 2	1 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bladder obstruction			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hydronephrosis			
subjects affected / exposed	0 / 852 (0.00%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nephropathy toxic			
subjects affected / exposed	0 / 852 (0.00%)	0 / 850 (0.00%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oliguria			
subjects affected / exposed	0 / 852 (0.00%)	0 / 850 (0.00%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
Adrenal insufficiency			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypercalcaemia of malignancy			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperparathyroidism primary			

subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Steroid withdrawal syndrome			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Adrenocortical insufficiency acute			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperthyroidism			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	5 / 852 (0.59%)	3 / 850 (0.35%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 5	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arthritis			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Back pain			
subjects affected / exposed	16 / 852 (1.88%)	9 / 850 (1.06%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 19	0 / 13	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bone pain			
subjects affected / exposed	7 / 852 (0.82%)	1 / 850 (0.12%)	3 / 418 (0.72%)
occurrences causally related to treatment / all	1 / 7	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Flank pain			

subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intervertebral disc protrusion			
subjects affected / exposed	2 / 852 (0.23%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Joint effusion			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lumbar spinal stenosis			
subjects affected / exposed	2 / 852 (0.23%)	0 / 850 (0.00%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Muscular weakness			
subjects affected / exposed	3 / 852 (0.35%)	3 / 850 (0.35%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	1 / 3	0 / 3	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Musculoskeletal chest pain			
subjects affected / exposed	2 / 852 (0.23%)	2 / 850 (0.24%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal discomfort			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal pain			
subjects affected / exposed	2 / 852 (0.23%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myalgia			

subjects affected / exposed	1 / 852 (0.12%)	2 / 850 (0.24%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neck pain			
subjects affected / exposed	2 / 852 (0.23%)	2 / 850 (0.24%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteonecrosis			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteonecrosis of jaw			
subjects affected / exposed	13 / 852 (1.53%)	18 / 850 (2.12%)	11 / 418 (2.63%)
occurrences causally related to treatment / all	13 / 14	18 / 18	10 / 11
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain in extremity			
subjects affected / exposed	5 / 852 (0.59%)	3 / 850 (0.35%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 5	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pathological fracture			
subjects affected / exposed	0 / 852 (0.00%)	2 / 850 (0.24%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal osteoarthritis			
subjects affected / exposed	2 / 852 (0.23%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal pain			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spondylolisthesis			

subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tendonitis			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vertebral lesion			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bone lesion			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bone swelling			
subjects affected / exposed	0 / 852 (0.00%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Costochondritis			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intervertebral disc disorder			
subjects affected / exposed	0 / 852 (0.00%)	0 / 850 (0.00%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mobility decreased			
subjects affected / exposed	0 / 852 (0.00%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteoarthritis			

subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteolysis			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Periarthritis			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Abscess bacterial			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Adenoviral haemorrhagic cystitis			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis			
subjects affected / exposed	3 / 852 (0.35%)	2 / 850 (0.24%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 3	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arthritis bacterial			
subjects affected / exposed	1 / 852 (0.12%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arthritis infective			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atypical pneumonia			

subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Bacteraemia			
subjects affected / exposed	2 / 852 (0.23%)	1 / 850 (0.12%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bacterial infection			
subjects affected / exposed	1 / 852 (0.12%)	3 / 850 (0.35%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bacterial pyelonephritis			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bacterial sepsis			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchiolitis			
subjects affected / exposed	2 / 852 (0.23%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	7 / 852 (0.82%)	11 / 850 (1.29%)	4 / 418 (0.96%)
occurrences causally related to treatment / all	0 / 7	0 / 11	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Bursitis infective			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			

subjects affected / exposed	5 / 852 (0.59%)	4 / 850 (0.47%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 6	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis orbital			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis infective			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic sinusitis			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium bacteraemia			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium difficile colitis			
subjects affected / exposed	4 / 852 (0.47%)	6 / 850 (0.71%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 6	0 / 6	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium difficile infection			
subjects affected / exposed	0 / 852 (0.00%)	3 / 850 (0.35%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Creutzfeldt-Jakob disease			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Cystitis			

subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cytomegalovirus chorioretinitis			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cytomegalovirus infection			
subjects affected / exposed	1 / 852 (0.12%)	2 / 850 (0.24%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device related infection			
subjects affected / exposed	2 / 852 (0.23%)	3 / 850 (0.35%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 2	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea infectious			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis			
subjects affected / exposed	1 / 852 (0.12%)	3 / 850 (0.35%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 2	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Encephalitis			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Erysipelas			
subjects affected / exposed	2 / 852 (0.23%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Escherichia sepsis			

subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Escherichia urinary tract infection			
subjects affected / exposed	1 / 852 (0.12%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Extradural abscess			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile infection			
subjects affected / exposed	2 / 852 (0.23%)	2 / 850 (0.24%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Folliculitis			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	3 / 852 (0.35%)	1 / 850 (0.12%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis viral			
subjects affected / exposed	0 / 852 (0.00%)	2 / 850 (0.24%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gingivitis			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes zoster			

subjects affected / exposed	9 / 852 (1.06%)	5 / 850 (0.59%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 9	0 / 6	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Human herpesvirus 6 infection			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infection			
subjects affected / exposed	0 / 852 (0.00%)	3 / 850 (0.35%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Infection in an immunocompromised host			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infection reactivation			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infective exacerbation of chronic obstructive airways disease			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza			
subjects affected / exposed	6 / 852 (0.70%)	10 / 850 (1.18%)	3 / 418 (0.72%)
occurrences causally related to treatment / all	0 / 6	0 / 10	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Intervertebral discitis			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower respiratory tract infection			

subjects affected / exposed	12 / 852 (1.41%)	5 / 850 (0.59%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 16	0 / 5	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Lower respiratory tract infection fungal			
subjects affected / exposed	1 / 852 (0.12%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower respiratory tract infection viral			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung infection			
subjects affected / exposed	0 / 852 (0.00%)	2 / 850 (0.24%)	2 / 418 (0.48%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meningitis meningococcal			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Meningitis pneumococcal			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Necrotising fasciitis			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenic infection			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenic sepsis			

subjects affected / exposed	3 / 852 (0.35%)	2 / 850 (0.24%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteomyelitis			
subjects affected / exposed	1 / 852 (0.12%)	3 / 850 (0.35%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 1	2 / 3	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Otitis media			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Parainfluenzae virus infection			
subjects affected / exposed	3 / 852 (0.35%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Perineal abscess			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Periodontitis			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peritonitis			
subjects affected / exposed	0 / 852 (0.00%)	2 / 850 (0.24%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Peritonsillar abscess			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumococcal sepsis			

subjects affected / exposed	1 / 852 (0.12%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumocystis jirovecii infection			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumocystis jirovecii pneumonia			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	82 / 852 (9.62%)	79 / 850 (9.29%)	34 / 418 (8.13%)
occurrences causally related to treatment / all	0 / 114	2 / 95	1 / 45
deaths causally related to treatment / all	0 / 11	0 / 6	0 / 3
Pneumonia bacterial			
subjects affected / exposed	0 / 852 (0.00%)	2 / 850 (0.24%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia klebsiella			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia legionella			
subjects affected / exposed	1 / 852 (0.12%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia pneumococcal			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia respiratory syncytial viral			

subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia staphylococcal			
subjects affected / exposed	1 / 852 (0.12%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia viral			
subjects affected / exposed	1 / 852 (0.12%)	1 / 850 (0.12%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural infection			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural sepsis			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Postoperative wound infection			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pseudomonal sepsis			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary mycosis			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory tract infection			

subjects affected / exposed	8 / 852 (0.94%)	7 / 850 (0.82%)	8 / 418 (1.91%)
occurrences causally related to treatment / all	0 / 10	0 / 8	0 / 8
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 0
Respiratory tract infection fungal			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory tract infection viral			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Salmonellosis			
subjects affected / exposed	1 / 852 (0.12%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Scrotal abscess			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	24 / 852 (2.82%)	19 / 850 (2.24%)	8 / 418 (1.91%)
occurrences causally related to treatment / all	1 / 31	0 / 21	0 / 9
deaths causally related to treatment / all	0 / 9	0 / 2	0 / 3
Sepsis syndrome			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Septic necrosis			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic shock			

subjects affected / exposed	7 / 852 (0.82%)	6 / 850 (0.71%)	7 / 418 (1.67%)
occurrences causally related to treatment / all	0 / 7	0 / 8	0 / 9
deaths causally related to treatment / all	0 / 2	0 / 4	0 / 4
Sinusitis			
subjects affected / exposed	2 / 852 (0.23%)	2 / 850 (0.24%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal cord infection			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Staphylococcal bacteraemia			
subjects affected / exposed	2 / 852 (0.23%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Staphylococcal sepsis			
subjects affected / exposed	2 / 852 (0.23%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Staphylococcal skin infection			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tonsillitis			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tracheobronchitis			
subjects affected / exposed	0 / 852 (0.00%)	2 / 850 (0.24%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			

subjects affected / exposed	2 / 852 (0.23%)	7 / 850 (0.82%)	2 / 418 (0.48%)
occurrences causally related to treatment / all	0 / 2	0 / 7	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	9 / 852 (1.06%)	6 / 850 (0.71%)	2 / 418 (0.48%)
occurrences causally related to treatment / all	0 / 9	0 / 10	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection bacterial			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urosepsis			
subjects affected / exposed	1 / 852 (0.12%)	3 / 850 (0.35%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Varicella			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral infection			
subjects affected / exposed	3 / 852 (0.35%)	2 / 850 (0.24%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 3	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral myositis			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound infection			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal abscess			

subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abscess jaw			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abscess neck			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abscess soft tissue			
subjects affected / exposed	0 / 852 (0.00%)	0 / 850 (0.00%)	2 / 418 (0.48%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute sinusitis			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bacterial parotitis			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchopulmonary aspergillosis			
subjects affected / exposed	0 / 852 (0.00%)	0 / 850 (0.00%)	2 / 418 (0.48%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Campylobacter gastroenteritis			
subjects affected / exposed	0 / 852 (0.00%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Candida infection			

subjects affected / exposed	0 / 852 (0.00%)	0 / 850 (0.00%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device related sepsis			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Empyema			
subjects affected / exposed	0 / 852 (0.00%)	0 / 850 (0.00%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Endocarditis			
subjects affected / exposed	0 / 852 (0.00%)	0 / 850 (0.00%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enterocolitis bacterial			
subjects affected / exposed	0 / 852 (0.00%)	0 / 850 (0.00%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epiglottitis			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gangrene			
subjects affected / exposed	0 / 852 (0.00%)	0 / 850 (0.00%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis norovirus			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis salmonella			

subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal infection			
subjects affected / exposed	0 / 852 (0.00%)	0 / 850 (0.00%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatitis B			
subjects affected / exposed	0 / 852 (0.00%)	0 / 850 (0.00%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes virus infection			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes zoster cutaneous disseminated			
subjects affected / exposed	0 / 852 (0.00%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infected dermal cyst			
subjects affected / exposed	0 / 852 (0.00%)	0 / 850 (0.00%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestine infection			
subjects affected / exposed	1 / 852 (0.12%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meningitis			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meningitis cryptococcal			

subjects affected / exposed	0 / 852 (0.00%)	0 / 850 (0.00%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metapneumovirus infection			
subjects affected / exposed	0 / 852 (0.00%)	0 / 850 (0.00%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nasopharyngitis			
subjects affected / exposed	0 / 852 (0.00%)	0 / 850 (0.00%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Opportunistic infection			
subjects affected / exposed	0 / 852 (0.00%)	0 / 850 (0.00%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Otitis externa			
subjects affected / exposed	0 / 852 (0.00%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Parvovirus B19 infection			
subjects affected / exposed	0 / 852 (0.00%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural infection			
subjects affected / exposed	0 / 852 (0.00%)	0 / 850 (0.00%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia fungal			
subjects affected / exposed	0 / 852 (0.00%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia haemophilus			

subjects affected / exposed	0 / 852 (0.00%)	0 / 850 (0.00%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia pseudomonal			
subjects affected / exposed	0 / 852 (0.00%)	0 / 850 (0.00%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia streptococcal			
subjects affected / exposed	0 / 852 (0.00%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pseudomembranous colitis			
subjects affected / exposed	0 / 852 (0.00%)	0 / 850 (0.00%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Pulmonary sepsis			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Soft tissue infection			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection fungal			
subjects affected / exposed	0 / 852 (0.00%)	0 / 850 (0.00%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular device infection			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral upper respiratory tract infection			

subjects affected / exposed	0 / 852 (0.00%)	0 / 850 (0.00%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Cachexia			
subjects affected / exposed	1 / 852 (0.12%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Decreased appetite			
subjects affected / exposed	2 / 852 (0.23%)	2 / 850 (0.24%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dehydration			
subjects affected / exposed	12 / 852 (1.41%)	10 / 850 (1.18%)	3 / 418 (0.72%)
occurrences causally related to treatment / all	0 / 12	0 / 12	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Electrolyte imbalance			
subjects affected / exposed	1 / 852 (0.12%)	2 / 850 (0.24%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Failure to thrive			
subjects affected / exposed	3 / 852 (0.35%)	1 / 850 (0.12%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 4	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 2	0 / 1	0 / 0
Fluid imbalance			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gout			
subjects affected / exposed	2 / 852 (0.23%)	2 / 850 (0.24%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemosiderosis			

subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypercalcaemia			
subjects affected / exposed	8 / 852 (0.94%)	2 / 850 (0.24%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	1 / 9	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperglycaemia			
subjects affected / exposed	0 / 852 (0.00%)	3 / 850 (0.35%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperkalaemia			
subjects affected / exposed	0 / 852 (0.00%)	2 / 850 (0.24%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypernatraemia			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperproteinaemia			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperuricaemia			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypocalcaemia			
subjects affected / exposed	2 / 852 (0.23%)	8 / 850 (0.94%)	2 / 418 (0.48%)
occurrences causally related to treatment / all	1 / 2	7 / 8	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoglycaemia			

subjects affected / exposed	2 / 852 (0.23%)	3 / 850 (0.35%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 2	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypokalaemia			
subjects affected / exposed	7 / 852 (0.82%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 7	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemia			
subjects affected / exposed	3 / 852 (0.35%)	3 / 850 (0.35%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lactic acidosis			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tumour lysis syndrome			
subjects affected / exposed	1 / 852 (0.12%)	0 / 850 (0.00%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperglycaemic hyperosmolar nonketotic syndrome			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypomagnesaemia			
subjects affected / exposed	0 / 852 (0.00%)	0 / 850 (0.00%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypophosphataemia			
subjects affected / exposed	0 / 852 (0.00%)	0 / 850 (0.00%)	1 / 418 (0.24%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Obesity			

subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Steroid diabetes			
subjects affected / exposed	0 / 852 (0.00%)	1 / 850 (0.12%)	0 / 418 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	OL: Denosumab / Denosumab		
Total subjects affected by serious adverse events			
subjects affected / exposed	156 / 426 (36.62%)		
number of deaths (all causes)	48		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute myeloid leukaemia			
subjects affected / exposed	0 / 426 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Adenocarcinoma of colon			
subjects affected / exposed	0 / 426 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Adenocarcinoma pancreas			
subjects affected / exposed	0 / 426 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Basal cell carcinoma			
subjects affected / exposed	1 / 426 (0.23%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Basosquamous carcinoma of skin			
subjects affected / exposed	0 / 426 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Bladder cancer				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bladder cancer recurrent				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cervix carcinoma				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Chronic myelomonocytic leukaemia				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Colon cancer				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Colorectal cancer metastatic				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Diffuse large B-cell lymphoma				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Endometrial adenocarcinoma				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hepatocellular carcinoma				

subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Malignant melanoma				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Malignant neoplasm of pleura				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Malignant neoplasm of renal pelvis				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Malignant pleural effusion				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Meningioma				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Metastases to spine				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Neoplasm of orbit				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Neuroendocrine tumour				

subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Non-Hodgkin's lymphoma				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Non-small cell lung cancer stage I				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Paraproteinaemia				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Plasma cell leukaemia				
subjects affected / exposed	2 / 426 (0.47%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Plasma cell myeloma				
subjects affected / exposed	10 / 426 (2.35%)			
occurrences causally related to treatment / all	0 / 12			
deaths causally related to treatment / all	0 / 9			
Plasma cell myeloma recurrent				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Plasmacytoma				
subjects affected / exposed	5 / 426 (1.17%)			
occurrences causally related to treatment / all	0 / 7			
deaths causally related to treatment / all	0 / 2			
Prostate cancer				

subjects affected / exposed	1 / 426 (0.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Rectal adenocarcinoma				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Sarcoma				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Squamous cell carcinoma of lung				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Squamous cell carcinoma of skin				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Acute leukaemia				
subjects affected / exposed	2 / 426 (0.47%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 2			
Acute lymphocytic leukaemia				
subjects affected / exposed	1 / 426 (0.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Acute lymphocytic leukaemia recurrent				
subjects affected / exposed	1 / 426 (0.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Adenocarcinoma gastric				

subjects affected / exposed	1 / 426 (0.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Anaplastic large-cell lymphoma				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bone marrow tumour cell infiltration				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Breast cancer				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Clear cell renal cell carcinoma				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Glioblastoma multiforme				
subjects affected / exposed	1 / 426 (0.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Intraductal proliferative breast lesion				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lung adenocarcinoma				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Malignant neoplasm progression				

subjects affected / exposed	1 / 426 (0.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Metastases to bone				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Myelodysplastic syndrome				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Oropharyngeal cancer				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Prostate cancer metastatic				
subjects affected / exposed	1 / 426 (0.23%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 1			
Spinal cord neoplasm				
subjects affected / exposed	1 / 426 (0.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Squamous cell carcinoma				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Tumour pain				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vascular disorders				
Aortic aneurysm				

subjects affected / exposed	0 / 426 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Aortic aneurysm rupture			
subjects affected / exposed	0 / 426 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Aortic dissection			
subjects affected / exposed	0 / 426 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Aortic dissection rupture			
subjects affected / exposed	0 / 426 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Aortic thrombosis			
subjects affected / exposed	0 / 426 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Circulatory collapse			
subjects affected / exposed	0 / 426 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Deep vein thrombosis			
subjects affected / exposed	1 / 426 (0.23%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Essential hypertension			
subjects affected / exposed	0 / 426 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Haematoma			

subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypertension				
subjects affected / exposed	1 / 426 (0.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hypotension				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypovolaemic shock				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Orthostatic hypotension				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Peripheral arterial occlusive disease				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Peripheral artery aneurysm				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Peripheral ischaemia				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Superior vena cava syndrome				

subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Thrombophlebitis superficial				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Thrombosis				
subjects affected / exposed	1 / 426 (0.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Vasospasm				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Aortic stenosis				
subjects affected / exposed	1 / 426 (0.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Arterial disorder				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypertensive urgency				
subjects affected / exposed	1 / 426 (0.23%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Venous thrombosis				
subjects affected / exposed	1 / 426 (0.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Surgical and medical procedures				
Cataract operation				

subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Fistula repair				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Haematopoietic stem cell mobilisation				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Internal fixation of fracture				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Intra-uterine contraceptive device removal				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Knee arthroplasty				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Rehabilitation therapy				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Autologous haematopoietic stem cell transplant				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
General disorders and administration				

site conditions				
Asthenia				
subjects affected / exposed	5 / 426 (1.17%)			
occurrences causally related to treatment / all	0 / 5			
deaths causally related to treatment / all	0 / 0			
Chest pain				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Chills				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Death				
subjects affected / exposed	1 / 426 (0.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Disease progression				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Fatigue				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gait disturbance				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
General physical health deterioration				
subjects affected / exposed	6 / 426 (1.41%)			
occurrences causally related to treatment / all	0 / 6			
deaths causally related to treatment / all	0 / 1			
Generalised oedema				

subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hyperpyrexia				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hyperthermia				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Localised oedema				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Malaise				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Mucosal ulceration				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Multiple organ dysfunction syndrome				
subjects affected / exposed	1 / 426 (0.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Non-cardiac chest pain				
subjects affected / exposed	2 / 426 (0.47%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Oedema peripheral				

subjects affected / exposed	1 / 426 (0.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Performance status decreased				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pyrexia				
subjects affected / exposed	4 / 426 (0.94%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 0			
Sudden cardiac death				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Sudden death				
subjects affected / exposed	1 / 426 (0.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Oedema				
subjects affected / exposed	2 / 426 (0.47%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Systemic inflammatory response syndrome				
subjects affected / exposed	1 / 426 (0.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Immune system disorders				
Acute graft versus host disease				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Acute graft versus host disease in intestine				

subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Anaphylactic reaction				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypersensitivity				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Serum sickness				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Reproductive system and breast disorders				
Adenomyosis				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Benign prostatic hyperplasia				
subjects affected / exposed	1 / 426 (0.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Scrotal oedema				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Testicular mass				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				

Acute pulmonary oedema				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Acute respiratory distress syndrome				
subjects affected / exposed	1 / 426 (0.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Acute respiratory failure				
subjects affected / exposed	1 / 426 (0.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Aspiration				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Asthma				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bronchial obstruction				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bronchopneumopathy				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Chronic obstructive pulmonary disease				
subjects affected / exposed	3 / 426 (0.70%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Cough				

subjects affected / exposed	1 / 426 (0.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Dyspnoea				
subjects affected / exposed	2 / 426 (0.47%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Epistaxis				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypoxia				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Interstitial lung disease				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lung disorder				
subjects affected / exposed	1 / 426 (0.23%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Nasal discomfort				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Non-cardiogenic pulmonary oedema				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pleural effusion				

subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia aspiration				
subjects affected / exposed	1 / 426 (0.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonitis				
subjects affected / exposed	1 / 426 (0.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumothorax				
subjects affected / exposed	1 / 426 (0.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Productive cough				
subjects affected / exposed	1 / 426 (0.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pulmonary artery thrombosis				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pulmonary embolism				
subjects affected / exposed	3 / 426 (0.70%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 1			
Pulmonary fibrosis				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pulmonary oedema				

subjects affected / exposed	3 / 426 (0.70%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 3			
Respiratory acidosis				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory distress				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory failure				
subjects affected / exposed	2 / 426 (0.47%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 2			
Stridor				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Asphyxia				
subjects affected / exposed	1 / 426 (0.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Bronchiectasis				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Dyspnoea exertional				
subjects affected / exposed	1 / 426 (0.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pleural disorder				

subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pleural thickening				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pleuritic pain				
subjects affected / exposed	1 / 426 (0.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pulmonary haemorrhage				
subjects affected / exposed	1 / 426 (0.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Pulmonary hypertension				
subjects affected / exposed	1 / 426 (0.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Psychiatric disorders				
Anxiety				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Completed suicide				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Confusional state				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Delirium				

subjects affected / exposed	2 / 426 (0.47%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Depression				
subjects affected / exposed	1 / 426 (0.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Disorientation				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Major depression				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Mental status changes				
subjects affected / exposed	1 / 426 (0.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Mutism				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Psychotic disorder				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Suicide attempt				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Adjustment disorder				

subjects affected / exposed	1 / 426 (0.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Drug dependence				
subjects affected / exposed	1 / 426 (0.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Organic brain syndrome				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Psychiatric decompensation				
subjects affected / exposed	1 / 426 (0.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Product issues				
Device breakage				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Device failure				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Device occlusion				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Device dislocation				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hepatobiliary disorders				

Acute hepatic failure				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bile duct stenosis				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cholangitis acute				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cholecystitis				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cholecystitis acute				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cholelithiasis				
subjects affected / exposed	1 / 426 (0.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Drug-induced liver injury				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hepatic function abnormal				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hepatitis toxic				

subjects affected / exposed	0 / 426 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hyperbilirubinaemia			
subjects affected / exposed	0 / 426 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Bile duct obstruction			
subjects affected / exposed	0 / 426 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cholecystitis chronic			
subjects affected / exposed	0 / 426 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gallbladder rupture			
subjects affected / exposed	0 / 426 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatic failure			
subjects affected / exposed	1 / 426 (0.23%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatitis			
subjects affected / exposed	0 / 426 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatotoxicity			
subjects affected / exposed	0 / 426 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Jaundice cholestatic			

subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Investigations				
Alanine aminotransferase increased				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Aspartate aminotransferase increased				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bilirubin conjugated increased				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Blood bilirubin increased				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Blood creatine increased				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Blood creatinine increased				
subjects affected / exposed	1 / 426 (0.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Blood electrolytes abnormal				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Blood immunoglobulin G increased				

subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Blood immunoglobulin M increased				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Blood lactate dehydrogenase increased				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Body temperature increased				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bone marrow plasmacyte count increased				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
C-reactive protein increased				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Chest X-ray abnormal				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Eastern Cooperative Oncology Group performance status worsened				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Haemoglobin decreased				

subjects affected / exposed	1 / 426 (0.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Heart rate irregular				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Light chain analysis increased				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Liver function test abnormal				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Monoclonal immunoglobulin present				
subjects affected / exposed	1 / 426 (0.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Neutrophil count decreased				
subjects affected / exposed	1 / 426 (0.23%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 0			
Platelet count decreased				
subjects affected / exposed	2 / 426 (0.47%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Weight decreased				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
White blood cell count decreased				

subjects affected / exposed	1 / 426 (0.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Blood immunoglobulin A increased				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Influenza A virus test positive				
subjects affected / exposed	1 / 426 (0.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Light chain analysis abnormal				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Plasma cells increased				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Plasma cells present				
subjects affected / exposed	1 / 426 (0.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Protein urine present				
subjects affected / exposed	1 / 426 (0.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
White blood cell count increased				
subjects affected / exposed	1 / 426 (0.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Injury, poisoning and procedural complications				
Abdominal injury				

subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Anastomotic leak				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bone contusion				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Brain contusion				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cervical vertebral fracture				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Concussion				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Fall				
subjects affected / exposed	3 / 426 (0.70%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Femoral neck fracture				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Femur fracture				

subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Fibula fracture				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hand fracture				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Head injury				
subjects affected / exposed	1 / 426 (0.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hip fracture				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Humerus fracture				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Joint dislocation				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lumbar vertebral fracture				
subjects affected / exposed	1 / 426 (0.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Patella fracture				

subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Post procedural haemorrhage				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Procedural pain				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Rib fracture				
subjects affected / exposed	2 / 426 (0.47%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Spinal compression fracture				
subjects affected / exposed	3 / 426 (0.70%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Spinal fracture				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Sternal fracture				
subjects affected / exposed	1 / 426 (0.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Subdural haematoma				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Tendon rupture				

subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Thoracic vertebral fracture				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Tibia fracture				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Transfusion related complication				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ankle fracture				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Compression fracture				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Craniocerebral injury				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Facial bones fracture				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Incarcerated incisional hernia				

subjects affected / exposed	1 / 426 (0.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Infusion related reaction				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Injury				
subjects affected / exposed	1 / 426 (0.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Limb fracture				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Poisoning				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Post procedural fever				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Procedural nausea				
subjects affected / exposed	1 / 426 (0.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pulmonary contusion				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Skin laceration				

subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Wound dehiscence				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Congenital, familial and genetic disorders				
Aplasia				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Odontogenic cyst				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
Acute coronary syndrome				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Acute myocardial infarction				
subjects affected / exposed	1 / 426 (0.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Angina pectoris				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Angina unstable				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Atrial fibrillation				
subjects affected / exposed	1 / 426 (0.23%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Atrial flutter				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Atrial tachycardia				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bradycardia				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac amyloidosis				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac arrest				
subjects affected / exposed	1 / 426 (0.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Cardiac disorder				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac failure				
subjects affected / exposed	4 / 426 (0.94%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 0			
Cardiac failure acute				

subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac failure chronic				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac failure congestive				
subjects affected / exposed	3 / 426 (0.70%)			
occurrences causally related to treatment / all	0 / 5			
deaths causally related to treatment / all	0 / 0			
Cardio-respiratory arrest				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiopulmonary failure				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiovascular insufficiency				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Coronary artery disease				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Left ventricular failure				
subjects affected / exposed	1 / 426 (0.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Mitral valve stenosis				

subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Myocardial infarction				
subjects affected / exposed	2 / 426 (0.47%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 2			
Myocardial ischaemia				
subjects affected / exposed	1 / 426 (0.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Myocarditis				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Palpitations				
subjects affected / exposed	1 / 426 (0.23%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Pericarditis				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Sinus bradycardia				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Sinus node dysfunction				
subjects affected / exposed	1 / 426 (0.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Sinus tachycardia				

subjects affected / exposed	0 / 426 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Supraventricular tachycardia			
subjects affected / exposed	1 / 426 (0.23%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Tachyarrhythmia			
subjects affected / exposed	0 / 426 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Tachycardia			
subjects affected / exposed	0 / 426 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Tricuspid valve incompetence			
subjects affected / exposed	0 / 426 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Acute left ventricular failure			
subjects affected / exposed	0 / 426 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Arrhythmia			
subjects affected / exposed	1 / 426 (0.23%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac tamponade			
subjects affected / exposed	0 / 426 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac valve disease			

subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiomyopathy				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Left ventricular dysfunction				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pericardial effusion				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ventricular arrhythmia				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
Basilar migraine				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Brain injury				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cauda equina syndrome				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cerebral haemorrhage				

subjects affected / exposed	1 / 426 (0.23%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 1			
Cerebral ischaemia				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cerebral vasoconstriction				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cerebrovascular accident				
subjects affected / exposed	1 / 426 (0.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cognitive disorder				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Coma				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Depressed level of consciousness				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Dizziness				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Encephalopathy				

subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Epilepsy				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Generalised tonic-clonic seizure				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Haemorrhage intracranial				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Haemorrhagic stroke				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hemiparesis				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hemiplegia				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypoaesthesia				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ischaemic cerebral infarction				

subjects affected / exposed	0 / 426 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Ischaemic stroke			
subjects affected / exposed	1 / 426 (0.23%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Lacunar infarction			
subjects affected / exposed	0 / 426 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Loss of consciousness			
subjects affected / exposed	0 / 426 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Lumbosacral radiculopathy			
subjects affected / exposed	0 / 426 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nerve degeneration			
subjects affected / exposed	0 / 426 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Neuropathy peripheral			
subjects affected / exposed	0 / 426 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Paralysis			
subjects affected / exposed	0 / 426 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Paraparesis			

subjects affected / exposed	0 / 426 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Paraplegia			
subjects affected / exposed	0 / 426 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Paresis			
subjects affected / exposed	0 / 426 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Polyneuropathy			
subjects affected / exposed	0 / 426 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Presyncope			
subjects affected / exposed	0 / 426 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Radiculopathy			
subjects affected / exposed	0 / 426 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Sciatica			
subjects affected / exposed	0 / 426 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Seizure			
subjects affected / exposed	1 / 426 (0.23%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Seizure like phenomena			

subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Spinal cord compression				
subjects affected / exposed	1 / 426 (0.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Subarachnoid haemorrhage				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Syncope				
subjects affected / exposed	2 / 426 (0.47%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Transient ischaemic attack				
subjects affected / exposed	1 / 426 (0.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Brain oedema				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cerebral atrophy				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cerebral haematoma				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cerebral infarction				

subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cerebrovascular disorder				
subjects affected / exposed	1 / 426 (0.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cervical cord compression				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Dementia				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Encephalitis post varicella				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Headache				
subjects affected / exposed	1 / 426 (0.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Intracranial mass				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Myelopathy				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Parkinson's disease				

subjects affected / exposed	0 / 426 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Agranulocytosis			
subjects affected / exposed	0 / 426 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Anaemia			
subjects affected / exposed	8 / 426 (1.88%)		
occurrences causally related to treatment / all	0 / 13		
deaths causally related to treatment / all	0 / 0		
Autoimmune haemolytic anaemia			
subjects affected / exposed	0 / 426 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Bicytopenia			
subjects affected / exposed	0 / 426 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Bone marrow failure			
subjects affected / exposed	0 / 426 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Febrile neutropenia			
subjects affected / exposed	6 / 426 (1.41%)		
occurrences causally related to treatment / all	0 / 6		
deaths causally related to treatment / all	0 / 0		
Haemolytic anaemia			
subjects affected / exposed	0 / 426 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hyperviscosity syndrome			

subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Leukocytosis				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Leukopenia				
subjects affected / exposed	1 / 426 (0.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Neutropenia				
subjects affected / exposed	3 / 426 (0.70%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Pancytopenia				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Thrombocytopenia				
subjects affected / exposed	7 / 426 (1.64%)			
occurrences causally related to treatment / all	0 / 13			
deaths causally related to treatment / all	0 / 0			
Acquired haemophilia with anti FVIII, XI, or XIII				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Anaemia of malignant disease				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cytopenia				

subjects affected / exposed	1 / 426 (0.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Platelet disorder				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Thrombocytosis				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ear and labyrinth disorders				
Vertigo				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vertigo positional				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Eye disorders				
Cataract				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Diplopia				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Exophthalmos				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Extraocular muscle paresis				

subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ulcerative keratitis				
subjects affected / exposed	1 / 426 (0.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Vision blurred				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
Abdominal discomfort				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Abdominal distension				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Abdominal hernia				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Abdominal incarcerated hernia				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Abdominal pain				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Abdominal pain lower				

subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Abdominal pain upper				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Abdominal wall haematoma				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Chronic gastritis				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Colitis				
subjects affected / exposed	1 / 426 (0.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Colitis ischaemic				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Constipation				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Diarrhoea				
subjects affected / exposed	4 / 426 (0.94%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 0			
Diarrhoea haemorrhagic				

subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Diverticulum intestinal				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Duodenal ulcer				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Duodenal ulcer haemorrhage				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Dysphagia				
subjects affected / exposed	1 / 426 (0.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Enteritis				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastritis				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastritis erosive				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal amyloidosis				

subjects affected / exposed	0 / 426 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal haemorrhage			
subjects affected / exposed	1 / 426 (0.23%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal perforation			
subjects affected / exposed	0 / 426 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gingivitis ulcerative			
subjects affected / exposed	0 / 426 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hiatus hernia			
subjects affected / exposed	0 / 426 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Ileus			
subjects affected / exposed	0 / 426 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Inguinal hernia			
subjects affected / exposed	3 / 426 (0.70%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Intestinal haemorrhage			
subjects affected / exposed	0 / 426 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Intestinal obstruction			

subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Large intestinal obstruction				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Large intestine perforation				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Large intestine polyp				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lower gastrointestinal haemorrhage				
subjects affected / exposed	2 / 426 (0.47%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Mechanical ileus				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Melaena				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Mouth haemorrhage				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nausea				

subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Oesophagitis				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pancreatitis				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Proctitis				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Rectal haemorrhage				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Small intestinal obstruction				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Stomatitis				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Subileus				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Umbilical hernia				

subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vomiting				
subjects affected / exposed	3 / 426 (0.70%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Anal fissure				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Appendiceal mucocoele				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Crohn's disease				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Dyspepsia				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastric ulcer haemorrhage				
subjects affected / exposed	1 / 426 (0.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal pain				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastrooesophageal reflux disease				

subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gingival bleeding				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Intestinal ischaemia				
subjects affected / exposed	1 / 426 (0.23%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 1			
Jejunal perforation				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Large intestinal haemorrhage				
subjects affected / exposed	1 / 426 (0.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Obstructive pancreatitis				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Retroperitoneal mass				
subjects affected / exposed	1 / 426 (0.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Small intestinal perforation				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Toothache				

subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Upper gastrointestinal haemorrhage				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Skin and subcutaneous tissue disorders				
Drug eruption				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Erythema multiforme				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hyperhidrosis				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Keloid scar				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Purpura				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Rash				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Rash macular				

subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Rash maculo-papular				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Skin disorder				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Urticaria				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Angioedema				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Decubitus ulcer				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Rash generalised				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Skin ulcer				
subjects affected / exposed	1 / 426 (0.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Renal and urinary disorders				
Acute kidney injury				

subjects affected / exposed	2 / 426 (0.47%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Bladder perforation				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Chronic kidney disease				
subjects affected / exposed	1 / 426 (0.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cystitis haemorrhagic				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Dysuria				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Haematuria				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nephrolithiasis				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Renal colic				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Renal disorder				

subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Renal failure				
subjects affected / exposed	6 / 426 (1.41%)			
occurrences causally related to treatment / all	0 / 7			
deaths causally related to treatment / all	0 / 1			
Renal impairment				
subjects affected / exposed	1 / 426 (0.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Ureteric obstruction				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ureterolithiasis				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Urinary retention				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bladder obstruction				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hydronephrosis				
subjects affected / exposed	1 / 426 (0.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Nephropathy toxic				

subjects affected / exposed	0 / 426 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Oliguria			
subjects affected / exposed	0 / 426 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Endocrine disorders			
Adrenal insufficiency			
subjects affected / exposed	0 / 426 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypercalcaemia of malignancy			
subjects affected / exposed	0 / 426 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hyperparathyroidism primary			
subjects affected / exposed	0 / 426 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Steroid withdrawal syndrome			
subjects affected / exposed	0 / 426 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Adrenocortical insufficiency acute			
subjects affected / exposed	0 / 426 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hyperthyroidism			
subjects affected / exposed	0 / 426 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			

Arthralgia			
subjects affected / exposed	0 / 426 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Arthritis			
subjects affected / exposed	0 / 426 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Back pain			
subjects affected / exposed	1 / 426 (0.23%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Bone pain			
subjects affected / exposed	0 / 426 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Flank pain			
subjects affected / exposed	0 / 426 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Intervertebral disc protrusion			
subjects affected / exposed	0 / 426 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Joint effusion			
subjects affected / exposed	0 / 426 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Lumbar spinal stenosis			
subjects affected / exposed	0 / 426 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Muscular weakness			

subjects affected / exposed	1 / 426 (0.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal chest pain				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal discomfort				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal pain				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Myalgia				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Neck pain				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Osteonecrosis				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Osteonecrosis of jaw				
subjects affected / exposed	12 / 426 (2.82%)			
occurrences causally related to treatment / all	12 / 13			
deaths causally related to treatment / all	0 / 0			
Pain in extremity				

subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pathological fracture				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Spinal osteoarthritis				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Spinal pain				
subjects affected / exposed	1 / 426 (0.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Spondylolisthesis				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Tendonitis				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vertebral lesion				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bone lesion				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bone swelling				

subjects affected / exposed	1 / 426 (0.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Costochondritis				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Intervertebral disc disorder				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Mobility decreased				
subjects affected / exposed	1 / 426 (0.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Osteoarthritis				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Osteolysis				
subjects affected / exposed	1 / 426 (0.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Periarthritis				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Abscess bacterial				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Adenoviral haemorrhagic cystitis				

subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Appendicitis				
subjects affected / exposed	1 / 426 (0.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Arthritis bacterial				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Arthritis infective				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Atypical pneumonia				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bacteraemia				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bacterial infection				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bacterial pyelonephritis				
subjects affected / exposed	1 / 426 (0.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Bacterial sepsis				

subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bronchiolitis				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bronchitis				
subjects affected / exposed	2 / 426 (0.47%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Bursitis infective				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cellulitis				
subjects affected / exposed	4 / 426 (0.94%)			
occurrences causally related to treatment / all	1 / 4			
deaths causally related to treatment / all	0 / 0			
Cellulitis orbital				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cholecystitis infective				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Chronic sinusitis				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Clostridium bacteraemia				

subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Clostridium difficile colitis				
subjects affected / exposed	2 / 426 (0.47%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Clostridium difficile infection				
subjects affected / exposed	1 / 426 (0.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Creutzfeldt-Jakob disease				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cystitis				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cytomegalovirus chorioretinitis				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cytomegalovirus infection				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Device related infection				
subjects affected / exposed	1 / 426 (0.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Diarrhoea infectious				

subjects affected / exposed	0 / 426 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Diverticulitis			
subjects affected / exposed	1 / 426 (0.23%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Encephalitis			
subjects affected / exposed	0 / 426 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Erysipelas			
subjects affected / exposed	0 / 426 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Escherichia sepsis			
subjects affected / exposed	0 / 426 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Escherichia urinary tract infection			
subjects affected / exposed	0 / 426 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Extradural abscess			
subjects affected / exposed	0 / 426 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Febrile infection			
subjects affected / exposed	0 / 426 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Folliculitis			

subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis				
subjects affected / exposed	2 / 426 (0.47%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis viral				
subjects affected / exposed	1 / 426 (0.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gingivitis				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Herpes zoster				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Human herpesvirus 6 infection				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Infection				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Infection in an immunocompromised host				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Infection reactivation				

subjects affected / exposed	0 / 426 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infective exacerbation of chronic obstructive airways disease			
subjects affected / exposed	0 / 426 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Influenza			
subjects affected / exposed	5 / 426 (1.17%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 0		
Intervertebral discitis			
subjects affected / exposed	0 / 426 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Lower respiratory tract infection			
subjects affected / exposed	1 / 426 (0.23%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Lower respiratory tract infection fungal			
subjects affected / exposed	0 / 426 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Lower respiratory tract infection viral			
subjects affected / exposed	0 / 426 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Lung infection			
subjects affected / exposed	1 / 426 (0.23%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Meningitis meningococcal			

subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Meningitis pneumococcal				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Necrotising fasciitis				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Neutropenic infection				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Neutropenic sepsis				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Osteomyelitis				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Otitis media				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Parainfluenzae virus infection				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Perineal abscess				

subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Periodontitis				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Peritonitis				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Peritonsillar abscess				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumococcal sepsis				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumocystis jirovecii infection				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumocystis jirovecii pneumonia				
subjects affected / exposed	1 / 426 (0.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia				
subjects affected / exposed	31 / 426 (7.28%)			
occurrences causally related to treatment / all	0 / 46			
deaths causally related to treatment / all	0 / 8			
Pneumonia bacterial				

subjects affected / exposed	1 / 426 (0.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia klebsiella				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia legionella				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia pneumococcal				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia respiratory syncytial viral				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia staphylococcal				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia viral				
subjects affected / exposed	1 / 426 (0.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Post procedural infection				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Post procedural sepsis				

subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Postoperative wound infection				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pseudomonal sepsis				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pulmonary mycosis				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory tract infection				
subjects affected / exposed	5 / 426 (1.17%)			
occurrences causally related to treatment / all	0 / 6			
deaths causally related to treatment / all	0 / 0			
Respiratory tract infection fungal				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory tract infection viral				
subjects affected / exposed	1 / 426 (0.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Salmonellosis				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Scrotal abscess				

subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Sepsis				
subjects affected / exposed	11 / 426 (2.58%)			
occurrences causally related to treatment / all	0 / 17			
deaths causally related to treatment / all	0 / 3			
Sepsis syndrome				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Septic necrosis				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Septic shock				
subjects affected / exposed	2 / 426 (0.47%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Sinusitis				
subjects affected / exposed	1 / 426 (0.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Spinal cord infection				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Staphylococcal bacteraemia				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Staphylococcal sepsis				

subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Staphylococcal skin infection				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Tonsillitis				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Tracheobronchitis				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Upper respiratory tract infection				
subjects affected / exposed	2 / 426 (0.47%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Urinary tract infection				
subjects affected / exposed	1 / 426 (0.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Urinary tract infection bacterial				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Urosepsis				
subjects affected / exposed	1 / 426 (0.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Varicella				

subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Viral infection				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Viral myositis				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Wound infection				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Abdominal abscess				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Abscess jaw				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Abscess neck				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Abscess soft tissue				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Acute sinusitis				

subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bacterial parotitis				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bronchopulmonary aspergillosis				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Campylobacter gastroenteritis				
subjects affected / exposed	1 / 426 (0.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Candida infection				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Device related sepsis				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Empyema				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Endocarditis				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Enterocolitis bacterial				

subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Epiglottitis				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gangrene				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis norovirus				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis salmonella				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal infection				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hepatitis B				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Herpes virus infection				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Herpes zoster cutaneous disseminated				

subjects affected / exposed	1 / 426 (0.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Infected dermal cyst				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Large intestine infection				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Meningitis				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Meningitis cryptococcal				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Metapneumovirus infection				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nasopharyngitis				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Opportunistic infection				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Otitis externa				

subjects affected / exposed	1 / 426 (0.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Parvovirus B19 infection				
subjects affected / exposed	1 / 426 (0.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pleural infection				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia fungal				
subjects affected / exposed	1 / 426 (0.23%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 1			
Pneumonia haemophilus				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia pseudomonal				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia streptococcal				
subjects affected / exposed	1 / 426 (0.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pseudomembranous colitis				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pulmonary sepsis				

subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Soft tissue infection				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Urinary tract infection fungal				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vascular device infection				
subjects affected / exposed	1 / 426 (0.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Viral upper respiratory tract infection				
subjects affected / exposed	1 / 426 (0.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Metabolism and nutrition disorders				
Cachexia				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Decreased appetite				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Dehydration				
subjects affected / exposed	1 / 426 (0.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Electrolyte imbalance				

subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Failure to thrive				
subjects affected / exposed	1 / 426 (0.23%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 1			
Fluid imbalance				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gout				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Haemosiderosis				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypercalcaemia				
subjects affected / exposed	3 / 426 (0.70%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 0			
Hyperglycaemia				
subjects affected / exposed	1 / 426 (0.23%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hyperkalaemia				
subjects affected / exposed	0 / 426 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypernatraemia				

subjects affected / exposed	0 / 426 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hyperproteinaemia			
subjects affected / exposed	0 / 426 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hyperuricaemia			
subjects affected / exposed	0 / 426 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypocalcaemia			
subjects affected / exposed	2 / 426 (0.47%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Hypoglycaemia			
subjects affected / exposed	0 / 426 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypokalaemia			
subjects affected / exposed	2 / 426 (0.47%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Hyponatraemia			
subjects affected / exposed	0 / 426 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Lactic acidosis			
subjects affected / exposed	0 / 426 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Tumour lysis syndrome			

subjects affected / exposed	0 / 426 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hyperglycaemic hyperosmolar nonketotic syndrome			
subjects affected / exposed	0 / 426 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypomagnesaemia			
subjects affected / exposed	1 / 426 (0.23%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Hypophosphataemia			
subjects affected / exposed	1 / 426 (0.23%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Obesity			
subjects affected / exposed	0 / 426 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Steroid diabetes			
subjects affected / exposed	0 / 426 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	DB: Zoledronic Acid	DB: Denosumab	OL: Zoledronic Acid / Denosumab
Total subjects affected by non-serious adverse events			
subjects affected / exposed	778 / 852 (91.31%)	757 / 850 (89.06%)	313 / 418 (74.88%)
Vascular disorders			
Hypertension			
subjects affected / exposed	70 / 852 (8.22%)	63 / 850 (7.41%)	13 / 418 (3.11%)
occurrences (all)	101	83	18
Hypotension			

subjects affected / exposed	39 / 852 (4.58%)	50 / 850 (5.88%)	6 / 418 (1.44%)
occurrences (all)	43	57	6
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	128 / 852 (15.02%)	112 / 850 (13.18%)	26 / 418 (6.22%)
occurrences (all)	190	182	31
Fatigue			
subjects affected / exposed	215 / 852 (25.23%)	206 / 850 (24.24%)	43 / 418 (10.29%)
occurrences (all)	357	312	66
Mucosal inflammation			
subjects affected / exposed	55 / 852 (6.46%)	76 / 850 (8.94%)	5 / 418 (1.20%)
occurrences (all)	67	100	5
Oedema peripheral			
subjects affected / exposed	147 / 852 (17.25%)	152 / 850 (17.88%)	29 / 418 (6.94%)
occurrences (all)	208	226	31
Pyrexia			
subjects affected / exposed	210 / 852 (24.65%)	182 / 850 (21.41%)	30 / 418 (7.18%)
occurrences (all)	311	268	42
Pain			
subjects affected / exposed	39 / 852 (4.58%)	45 / 850 (5.29%)	5 / 418 (1.20%)
occurrences (all)	48	57	5
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	170 / 852 (19.95%)	159 / 850 (18.71%)	51 / 418 (12.20%)
occurrences (all)	261	228	63
Dyspnoea			
subjects affected / exposed	96 / 852 (11.27%)	83 / 850 (9.76%)	22 / 418 (5.26%)
occurrences (all)	130	117	27
Oropharyngeal pain			
subjects affected / exposed	46 / 852 (5.40%)	65 / 850 (7.65%)	13 / 418 (3.11%)
occurrences (all)	56	77	14
Psychiatric disorders			
Anxiety			
subjects affected / exposed	72 / 852 (8.45%)	61 / 850 (7.18%)	4 / 418 (0.96%)
occurrences (all)	83	68	4
Depression			

subjects affected / exposed	66 / 852 (7.75%)	47 / 850 (5.53%)	4 / 418 (0.96%)
occurrences (all)	73	54	4
Insomnia			
subjects affected / exposed	135 / 852 (15.85%)	132 / 850 (15.53%)	20 / 418 (4.78%)
occurrences (all)	174	171	22
Investigations			
Blood creatinine increased			
subjects affected / exposed	80 / 852 (9.39%)	36 / 850 (4.24%)	15 / 418 (3.59%)
occurrences (all)	136	54	31
Platelet count decreased			
subjects affected / exposed	55 / 852 (6.46%)	55 / 850 (6.47%)	10 / 418 (2.39%)
occurrences (all)	163	178	23
Weight decreased			
subjects affected / exposed	61 / 852 (7.16%)	61 / 850 (7.18%)	12 / 418 (2.87%)
occurrences (all)	78	80	12
Injury, poisoning and procedural complications			
Lumbar vertebral fracture			
subjects affected / exposed	72 / 852 (8.45%)	70 / 850 (8.24%)	1 / 418 (0.24%)
occurrences (all)	82	94	1
Rib fracture			
subjects affected / exposed	70 / 852 (8.22%)	69 / 850 (8.12%)	2 / 418 (0.48%)
occurrences (all)	118	119	2
Thoracic vertebral fracture			
subjects affected / exposed	75 / 852 (8.80%)	95 / 850 (11.18%)	0 / 418 (0.00%)
occurrences (all)	108	141	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	94 / 852 (11.03%)	92 / 850 (10.82%)	19 / 418 (4.55%)
occurrences (all)	119	121	19
Headache			
subjects affected / exposed	88 / 852 (10.33%)	100 / 850 (11.76%)	12 / 418 (2.87%)
occurrences (all)	124	145	17
Hypoaesthesia			
subjects affected / exposed	47 / 852 (5.52%)	52 / 850 (6.12%)	11 / 418 (2.63%)
occurrences (all)	58	72	15
Neuropathy peripheral			

subjects affected / exposed	147 / 852 (17.25%)	134 / 850 (15.76%)	17 / 418 (4.07%)
occurrences (all)	215	182	18
Paraesthesia			
subjects affected / exposed	73 / 852 (8.57%)	70 / 850 (8.24%)	12 / 418 (2.87%)
occurrences (all)	93	79	12
Peripheral sensory neuropathy			
subjects affected / exposed	73 / 852 (8.57%)	80 / 850 (9.41%)	12 / 418 (2.87%)
occurrences (all)	127	136	17
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	185 / 852 (21.71%)	208 / 850 (24.47%)	51 / 418 (12.20%)
occurrences (all)	472	678	164
Febrile neutropenia			
subjects affected / exposed	82 / 852 (9.62%)	89 / 850 (10.47%)	9 / 418 (2.15%)
occurrences (all)	92	97	10
Neutropenia			
subjects affected / exposed	166 / 852 (19.48%)	173 / 850 (20.35%)	40 / 418 (9.57%)
occurrences (all)	455	590	66
Thrombocytopenia			
subjects affected / exposed	151 / 852 (17.72%)	174 / 850 (20.47%)	27 / 418 (6.46%)
occurrences (all)	439	665	107
Leukopenia			
subjects affected / exposed	41 / 852 (4.81%)	47 / 850 (5.53%)	10 / 418 (2.39%)
occurrences (all)	104	163	40
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	49 / 852 (5.75%)	78 / 850 (9.18%)	16 / 418 (3.83%)
occurrences (all)	68	97	22
Constipation			
subjects affected / exposed	214 / 852 (25.12%)	207 / 850 (24.35%)	19 / 418 (4.55%)
occurrences (all)	298	296	21
Diarrhoea			
subjects affected / exposed	301 / 852 (35.33%)	304 / 850 (35.76%)	73 / 418 (17.46%)
occurrences (all)	516	507	103
Dyspepsia			

subjects affected / exposed	62 / 852 (7.28%)	60 / 850 (7.06%)	12 / 418 (2.87%)
occurrences (all)	85	83	12
Nausea			
subjects affected / exposed	274 / 852 (32.16%)	284 / 850 (33.41%)	32 / 418 (7.66%)
occurrences (all)	466	474	43
Stomatitis			
subjects affected / exposed	53 / 852 (6.22%)	63 / 850 (7.41%)	5 / 418 (1.20%)
occurrences (all)	64	77	7
Vomiting			
subjects affected / exposed	159 / 852 (18.66%)	147 / 850 (17.29%)	18 / 418 (4.31%)
occurrences (all)	238	211	25
Abdominal pain upper			
subjects affected / exposed	44 / 852 (5.16%)	42 / 850 (4.94%)	9 / 418 (2.15%)
occurrences (all)	56	47	9
Toothache			
subjects affected / exposed	45 / 852 (5.28%)	50 / 850 (5.88%)	27 / 418 (6.46%)
occurrences (all)	51	64	31
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	48 / 852 (5.63%)	56 / 850 (6.59%)	0 / 418 (0.00%)
occurrences (all)	65	74	0
Pruritus			
subjects affected / exposed	51 / 852 (5.99%)	54 / 850 (6.35%)	6 / 418 (1.44%)
occurrences (all)	69	64	6
Rash			
subjects affected / exposed	102 / 852 (11.97%)	132 / 850 (15.53%)	17 / 418 (4.07%)
occurrences (all)	135	174	19
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	118 / 852 (13.85%)	131 / 850 (15.41%)	44 / 418 (10.53%)
occurrences (all)	195	191	65
Back pain			
subjects affected / exposed	181 / 852 (21.24%)	194 / 850 (22.82%)	46 / 418 (11.00%)
occurrences (all)	262	268	64
Bone pain			

subjects affected / exposed	105 / 852 (12.32%)	99 / 850 (11.65%)	16 / 418 (3.83%)
occurrences (all)	145	128	19
Muscle spasms			
subjects affected / exposed	50 / 852 (5.87%)	63 / 850 (7.41%)	28 / 418 (6.70%)
occurrences (all)	71	89	31
Musculoskeletal pain			
subjects affected / exposed	82 / 852 (9.62%)	72 / 850 (8.47%)	20 / 418 (4.78%)
occurrences (all)	108	96	29
Myalgia			
subjects affected / exposed	55 / 852 (6.46%)	50 / 850 (5.88%)	15 / 418 (3.59%)
occurrences (all)	72	68	17
Pain in extremity			
subjects affected / exposed	138 / 852 (16.20%)	127 / 850 (14.94%)	29 / 418 (6.94%)
occurrences (all)	198	178	42
Musculoskeletal chest pain			
subjects affected / exposed	44 / 852 (5.16%)	42 / 850 (4.94%)	7 / 418 (1.67%)
occurrences (all)	52	46	9
Osteonecrosis of jaw			
subjects affected / exposed	24 / 852 (2.82%)	38 / 850 (4.47%)	22 / 418 (5.26%)
occurrences (all)	28	42	26
Infections and infestations			
Bronchitis			
subjects affected / exposed	72 / 852 (8.45%)	72 / 850 (8.47%)	31 / 418 (7.42%)
occurrences (all)	88	87	47
Herpes zoster			
subjects affected / exposed	68 / 852 (7.98%)	62 / 850 (7.29%)	13 / 418 (3.11%)
occurrences (all)	73	68	16
Nasopharyngitis			
subjects affected / exposed	79 / 852 (9.27%)	84 / 850 (9.88%)	42 / 418 (10.05%)
occurrences (all)	129	129	60
Respiratory tract infection			
subjects affected / exposed	53 / 852 (6.22%)	56 / 850 (6.59%)	25 / 418 (5.98%)
occurrences (all)	77	81	44
Upper respiratory tract infection			
subjects affected / exposed	127 / 852 (14.91%)	143 / 850 (16.82%)	62 / 418 (14.83%)
occurrences (all)	219	231	106

Urinary tract infection			
subjects affected / exposed	51 / 852 (5.99%)	63 / 850 (7.41%)	17 / 418 (4.07%)
occurrences (all)	68	88	17
Influenza			
subjects affected / exposed	33 / 852 (3.87%)	26 / 850 (3.06%)	23 / 418 (5.50%)
occurrences (all)	40	33	25
Pneumonia			
subjects affected / exposed	50 / 852 (5.87%)	41 / 850 (4.82%)	20 / 418 (4.78%)
occurrences (all)	63	45	22
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	166 / 852 (19.48%)	140 / 850 (16.47%)	12 / 418 (2.87%)
occurrences (all)	230	191	12
Hypocalcaemia			
subjects affected / exposed	99 / 852 (11.62%)	141 / 850 (16.59%)	27 / 418 (6.46%)
occurrences (all)	188	330	51
Hypokalaemia			
subjects affected / exposed	140 / 852 (16.43%)	129 / 850 (15.18%)	26 / 418 (6.22%)
occurrences (all)	292	224	51
Hypomagnesaemia			
subjects affected / exposed	52 / 852 (6.10%)	39 / 850 (4.59%)	7 / 418 (1.67%)
occurrences (all)	76	50	10
Hypophosphataemia			
subjects affected / exposed	48 / 852 (5.63%)	59 / 850 (6.94%)	15 / 418 (3.59%)
occurrences (all)	128	145	29

Non-serious adverse events	OL: Denosumab / Denosumab		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	312 / 426 (73.24%)		
Vascular disorders			
Hypertension			
subjects affected / exposed	16 / 426 (3.76%)		
occurrences (all)	18		
Hypotension			
subjects affected / exposed	7 / 426 (1.64%)		
occurrences (all)	10		
General disorders and administration			

site conditions			
Asthenia			
subjects affected / exposed	18 / 426 (4.23%)		
occurrences (all)	20		
Fatigue			
subjects affected / exposed	38 / 426 (8.92%)		
occurrences (all)	52		
Mucosal inflammation			
subjects affected / exposed	3 / 426 (0.70%)		
occurrences (all)	3		
Oedema peripheral			
subjects affected / exposed	14 / 426 (3.29%)		
occurrences (all)	18		
Pyrexia			
subjects affected / exposed	44 / 426 (10.33%)		
occurrences (all)	67		
Pain			
subjects affected / exposed	16 / 426 (3.76%)		
occurrences (all)	19		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	47 / 426 (11.03%)		
occurrences (all)	66		
Dyspnoea			
subjects affected / exposed	25 / 426 (5.87%)		
occurrences (all)	35		
Oropharyngeal pain			
subjects affected / exposed	12 / 426 (2.82%)		
occurrences (all)	16		
Psychiatric disorders			
Anxiety			
subjects affected / exposed	7 / 426 (1.64%)		
occurrences (all)	7		
Depression			
subjects affected / exposed	8 / 426 (1.88%)		
occurrences (all)	8		

Insomnia			
subjects affected / exposed	15 / 426 (3.52%)		
occurrences (all)	16		
Investigations			
Blood creatinine increased			
subjects affected / exposed	9 / 426 (2.11%)		
occurrences (all)	12		
Platelet count decreased			
subjects affected / exposed	14 / 426 (3.29%)		
occurrences (all)	35		
Weight decreased			
subjects affected / exposed	9 / 426 (2.11%)		
occurrences (all)	10		
Injury, poisoning and procedural complications			
Lumbar vertebral fracture			
subjects affected / exposed	1 / 426 (0.23%)		
occurrences (all)	1		
Rib fracture			
subjects affected / exposed	3 / 426 (0.70%)		
occurrences (all)	3		
Thoracic vertebral fracture			
subjects affected / exposed	1 / 426 (0.23%)		
occurrences (all)	1		
Nervous system disorders			
Dizziness			
subjects affected / exposed	14 / 426 (3.29%)		
occurrences (all)	16		
Headache			
subjects affected / exposed	19 / 426 (4.46%)		
occurrences (all)	25		
Hypoaesthesia			
subjects affected / exposed	9 / 426 (2.11%)		
occurrences (all)	9		
Neuropathy peripheral			
subjects affected / exposed	14 / 426 (3.29%)		
occurrences (all)	14		

Paraesthesia			
subjects affected / exposed	11 / 426 (2.58%)		
occurrences (all)	12		
Peripheral sensory neuropathy			
subjects affected / exposed	5 / 426 (1.17%)		
occurrences (all)	8		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	62 / 426 (14.55%)		
occurrences (all)	205		
Febrile neutropenia			
subjects affected / exposed	2 / 426 (0.47%)		
occurrences (all)	2		
Neutropenia			
subjects affected / exposed	51 / 426 (11.97%)		
occurrences (all)	162		
Thrombocytopenia			
subjects affected / exposed	27 / 426 (6.34%)		
occurrences (all)	115		
Leukopenia			
subjects affected / exposed	10 / 426 (2.35%)		
occurrences (all)	57		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	13 / 426 (3.05%)		
occurrences (all)	17		
Constipation			
subjects affected / exposed	27 / 426 (6.34%)		
occurrences (all)	35		
Diarrhoea			
subjects affected / exposed	57 / 426 (13.38%)		
occurrences (all)	102		
Dyspepsia			
subjects affected / exposed	11 / 426 (2.58%)		
occurrences (all)	14		
Nausea			

subjects affected / exposed	35 / 426 (8.22%)		
occurrences (all)	48		
Stomatitis			
subjects affected / exposed	8 / 426 (1.88%)		
occurrences (all)	11		
Vomiting			
subjects affected / exposed	19 / 426 (4.46%)		
occurrences (all)	23		
Abdominal pain upper			
subjects affected / exposed	6 / 426 (1.41%)		
occurrences (all)	7		
Toothache			
subjects affected / exposed	16 / 426 (3.76%)		
occurrences (all)	19		
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	4 / 426 (0.94%)		
occurrences (all)	5		
Pruritus			
subjects affected / exposed	12 / 426 (2.82%)		
occurrences (all)	13		
Rash			
subjects affected / exposed	17 / 426 (3.99%)		
occurrences (all)	23		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	36 / 426 (8.45%)		
occurrences (all)	48		
Back pain			
subjects affected / exposed	56 / 426 (13.15%)		
occurrences (all)	64		
Bone pain			
subjects affected / exposed	13 / 426 (3.05%)		
occurrences (all)	13		
Muscle spasms			

subjects affected / exposed	27 / 426 (6.34%)		
occurrences (all)	28		
Musculoskeletal pain			
subjects affected / exposed	23 / 426 (5.40%)		
occurrences (all)	29		
Myalgia			
subjects affected / exposed	6 / 426 (1.41%)		
occurrences (all)	6		
Pain in extremity			
subjects affected / exposed	28 / 426 (6.57%)		
occurrences (all)	32		
Musculoskeletal chest pain			
subjects affected / exposed	13 / 426 (3.05%)		
occurrences (all)	16		
Osteonecrosis of jaw			
subjects affected / exposed	36 / 426 (8.45%)		
occurrences (all)	41		
Infections and infestations			
Bronchitis			
subjects affected / exposed	32 / 426 (7.51%)		
occurrences (all)	41		
Herpes zoster			
subjects affected / exposed	5 / 426 (1.17%)		
occurrences (all)	5		
Nasopharyngitis			
subjects affected / exposed	38 / 426 (8.92%)		
occurrences (all)	54		
Respiratory tract infection			
subjects affected / exposed	26 / 426 (6.10%)		
occurrences (all)	36		
Upper respiratory tract infection			
subjects affected / exposed	58 / 426 (13.62%)		
occurrences (all)	104		
Urinary tract infection			
subjects affected / exposed	19 / 426 (4.46%)		
occurrences (all)	25		

Influenza			
subjects affected / exposed	23 / 426 (5.40%)		
occurrences (all)	30		
Pneumonia			
subjects affected / exposed	13 / 426 (3.05%)		
occurrences (all)	15		
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	12 / 426 (2.82%)		
occurrences (all)	13		
Hypocalcaemia			
subjects affected / exposed	30 / 426 (7.04%)		
occurrences (all)	62		
Hypokalaemia			
subjects affected / exposed	26 / 426 (6.10%)		
occurrences (all)	69		
Hypomagnesaemia			
subjects affected / exposed	9 / 426 (2.11%)		
occurrences (all)	21		
Hypophosphataemia			
subjects affected / exposed	12 / 426 (2.82%)		
occurrences (all)	27		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
18 August 2011	- specified that antimyeloma therapy (excluding bisphosphonates) could start before randomization if the subject has signed informed consent and screening blood samples have been collected for central analysis. Also, the first dose of investigational product was not linked to the initiation of antimyeloma therapy, and it could be before or after antimyeloma therapy was started. This permitted the initiation of antimyeloma therapy without delays because of the protocol screening process. - eliminated the requirement that the SC injection of blinded investigational product must be before the IV infusion of blinded investigational product - added citations and made modifications to the response criteria - clarified that serious adverse events would be submitted to Amgen using an electronic method - removed the PRO assessment on day 8 - made minor changes to exploratory endpoints and covariates
11 February 2013	- changed the assessments of myeloma disease response and progression from central analysis to local analysis as per standard of care in the management of multiple myeloma - permitted a limited duration of prior antimyeloma therapy before enrollment - reduced the number and timing of laboratory tests - reassigned the endpoint of progression-free survival from additional secondary to exploratory, and deleted exploratory endpoints related to disease response - modified the prestudy bisphosphonate exposure to allow a limited duration - provided additional guidance regarding investigational product dosing and oral/dental procedures - reduced the skeletal surveys after 3 years from every 12 weeks to every 24 weeks
12 August 2015	- increased the study sample size by 180 subjects and decreased power to 85% - deleted the trade name "Zometa" to allow for the use of branded or generic zoledronic acid supplied for the study - updated pregnancy and contraception language and included updated pregnancy and lactation notification worksheets - defined potentially unblinding test values that would remain blinded
18 December 2017	- updated information about the DMC meetings; after the DMC review of the primary analysis in July 2016, no further DMC meetings were to be held for this study (aligned with the expectations set forth in the DMC charter) - updated the schedule of assessment to provide information aligned to support the primary objectives of the open-label treatment period of the study

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported