



Clinical trial results:

A Phase 3, Randomized, Open Label Trial of Lenalidomide/dexamethasone With or Without Elotuzumab in Subjects with Previously Untreated Multiple Myeloma Summary

EudraCT number	2010-022445-20
Trial protocol	CZ HU IE GB DE ES BE AT GR IT PL
Global end of trial date	03 September 2021

Results information

Result version number	v1 (current)
This version publication date	20 September 2022
First version publication date	20 September 2022

Trial information

Trial identification

Sponsor protocol code	CA204-006
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Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Bristol-Myers Squibb
Sponsor organisation address	Chaussée de la Hulpe 185, Brussels, Belgium, 1170
Public contact	EU Study Start-Up Unit, Bristol-Myers Squibb International Corporation, Clinical.Trials@bms.com
Scientific contact	Bristol-Myers Squibb Study Director, Bristol-Myers Squibb, Clinical.Trials@bms.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	04 March 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	03 September 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To compare PFS of lenalidomide/dexamethasone + elotuzumab (E-Ld) versus lenalidomide/dexamethasone (Ld) in subjects with newly diagnosed, untreated multiple myeloma (MM).

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	18 May 2011
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 42
Country: Number of subjects enrolled	Austria: 7
Country: Number of subjects enrolled	Belgium: 20
Country: Number of subjects enrolled	Canada: 77
Country: Number of subjects enrolled	Czechia: 12
Country: Number of subjects enrolled	Germany: 35
Country: Number of subjects enrolled	Greece: 68
Country: Number of subjects enrolled	Hungary: 16
Country: Number of subjects enrolled	Ireland: 6
Country: Number of subjects enrolled	Israel: 28
Country: Number of subjects enrolled	Italy: 95
Country: Number of subjects enrolled	Poland: 72
Country: Number of subjects enrolled	Romania: 20
Country: Number of subjects enrolled	Russian Federation: 3
Country: Number of subjects enrolled	Spain: 53
Country: Number of subjects enrolled	Switzerland: 5
Country: Number of subjects enrolled	Turkey: 5
Country: Number of subjects enrolled	United Kingdom: 9
Country: Number of subjects enrolled	United States: 175

Worldwide total number of subjects	748
EEA total number of subjects	404

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)	40
From 65 to 84 years	677
85 years and over	31

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

- E-Ld cohort: 374 participants were randomized.
371 participants entered the treatment period.
- Ld cohort: 374 participants were randomized.
371 participants entered the treatment period.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
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Arm title	E-Ld cohort
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Arm description:

Participants receiving a combination of Elotuzumab (E) Lenalidomide (L) Dexamethasone (d) in a 28 day cycle

Arm type	Experimental
Investigational medicinal product name	Elotuzumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

20 mL Vial

Investigational medicinal product name	Lenalidomide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

5 mg, 10 mg, 15 mg and 25 mg Capsules

Investigational medicinal product name	Dexamethasone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

2 mg and 4 mg & various strengths

Investigational medicinal product name	Dexamethasone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravascular use

Dosage and administration details:

4 mg/ml, 8 mg/ml & various strengths

Arm title	Ld cohort
Arm description:	
Participants receiving a combination of Lenalidomide (L) Dexamethasone (d) in a 28 day cycle	
Arm type	Active comparator
Investigational medicinal product name	Lenalidomide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use
Dosage and administration details:	
5 mg, 10 mg, 15 mg and 25 mg Capsules	
Investigational medicinal product name	Dexamethasone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravascular use
Dosage and administration details:	
4 mg/ml, 8 mg/ml & various strengths	
Investigational medicinal product name	Dexamethasone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
2 mg and 4 mg & various strengths	

Number of subjects in period 1	E-Ld cohort	Ld cohort
Started	374	374
Completed	371	371
Not completed	3	3
Consent withdrawal	3	-
No longer meeting study criteria	-	1
Participant request to discontinue	-	1
Adverse event unrelated to study drug	-	1

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

Arms

Are arms mutually exclusive?	Yes
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Arm title	E-Ld cohort
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Arm description:

Participants receiving a combination of Elotuzumab (E) Lenalidomide (L) Dexamethasone (d) in a 28 day cycle

Arm type	Experimental
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Investigational medicinal product name	Elotuzumab
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Investigational medicinal product code	
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Other name	
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Pharmaceutical forms	Powder for solution for infusion
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Routes of administration	Intravascular use
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Dosage and administration details:

400 mg/vial

Investigational medicinal product name	Dexamethasone
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Investigational medicinal product code	
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Other name	
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Pharmaceutical forms	Tablet
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Routes of administration	Oral use
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Dosage and administration details:

2 mg and 4 mg & various strengths

Investigational medicinal product name	Dexamethasone
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Investigational medicinal product code	
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Other name	
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Pharmaceutical forms	Solution for infusion
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Routes of administration	Intravascular use
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Dosage and administration details:

4 mg/ml, 8 mg/ml & various strengths

Investigational medicinal product name	Lenalidomide
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Investigational medicinal product code	
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Other name	
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Pharmaceutical forms	Capsule
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Routes of administration	Oral use
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Dosage and administration details:

5 mg, 10 mg, 15 mg and 25 mg

Arm title	Ld cohort
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Arm description:

Participants receiving a combination of Lenalidomide (L) Dexamethasone (d) in a 28 day cycle

Arm type	Active comparator
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Investigational medicinal product name	Lenalidomide
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Investigational medicinal product code	
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Other name	
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Pharmaceutical forms	Capsule
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Routes of administration	Oral use
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Dosage and administration details:

5 mg, 10 mg, 15 mg and 25 mg

Investigational medicinal product name	Dexamethasone
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Investigational medicinal product code	
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Other name	
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Pharmaceutical forms	Tablet
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Routes of administration	Oral use
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Dosage and administration details:

2 mg and 4 mg & various strengths

Investigational medicinal product name	Dexamethosone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravascular use

Dosage and administration details:

4 mg/ml, 8 mg/ml & various strengths

Number of subjects in period 2	E-Ld cohort	Ld cohort
Started	371	371
Completed	0	0
Not completed	371	371
Adverse event, serious fatal	7	6
No longer meet study criteria	1	1
Disease progression	117	145
Consent withdrawal	10	7
Study drug toxicity	52	64
Participant request to discontinue	30	22
Maximum clinical benefit	1	1
Adverse event unrelated to study drug	110	73
Other reasons	30	30
Poor/Non-compliance	3	4
Administrative reasons by Sponsor	8	16
Lost to follow-up	2	2

Baseline characteristics

Reporting groups

Reporting group title	E-Ld cohort
Reporting group description:	
Participants receiving a combination of Elotuzumab (E) Lenalidomide (L) Dexamethasone (d) in a 28 day cycle	
Reporting group title	Ld cohort
Reporting group description:	
Participants receiving a combination of Lenalidomide (L) Dexamethasone (d) in a 28 day cycle	

Reporting group values	E-Ld cohort	Ld cohort	Total
Number of subjects	374	374	748
Age categorical			
Units: Subjects			
Adults (18-64 years)	20	20	40
From 65-84 years	341	336	677
85 years and over	13	18	31
Age Continuous			
Units: Years			
arithmetic mean	72.9	73.1	
standard deviation	± 6.58	± 6.70	-
Sex: Female, Male			
Units: Participants			
Female	163	173	336
Male	211	201	412
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	1	4	5
Native Hawaiian or Other Pacific Islander	0	1	1
Black or African American	13	16	29
White	360	351	711
More than one race	0	0	0
Unknown or Not Reported	0	2	2
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	9	8	17
Not Hispanic or Latino	70	87	157
Unknown or Not Reported	295	279	574

End points

End points reporting groups

Reporting group title	E-Ld cohort
Reporting group description:	
Participants receiving a combination of Elotuzumab (E) Lenalidomide (L) Dexamethasone (d) in a 28 day cycle	
Reporting group title	Ld cohort
Reporting group description:	
Participants receiving a combination of Lenalidomide (L) Dexamethasone (d) in a 28 day cycle	
Reporting group title	E-Ld cohort
Reporting group description:	
Participants receiving a combination of Elotuzumab (E) Lenalidomide (L) Dexamethasone (d) in a 28 day cycle	
Reporting group title	Ld cohort
Reporting group description:	
Participants receiving a combination of Lenalidomide (L) Dexamethasone (d) in a 28 day cycle	

Primary: Progression-Free Survival (PFS)

End point title	Progression-Free Survival (PFS)
End point description:	
PFS is defined as the time from randomization to the date of the first documented tumor progression (as determined by the Independent Review Committee (IRC)) or death due to any cause.	
The IRC conducted a blinded, independent review of the tumor assessments based on the European Group for Blood and Bone Marrow Transplant (EBMT) criteria.	
Censoring rules applied:	
- Participants receiving subsequent systemic anti-myeloma therapy prior to documented progression were censored at the date of the last adequate tumor assessment prior to new therapy.	
- Participants who had an event (progression or death) > 10 weeks after their last tumor assessment were censored at their last adequate tumor assessment prior to the event.	
- Participants without progression or death (and not receiving subsequent therapy prior to progression) were censored at their last adequate tumor assessment.	
- Participants without any post-baseline tumor assessments were censored on the date of randomization	
End point type	Primary
End point timeframe:	
From randomization to date of first documented tumor progression or death due to any cause (up to 8 years)	

End point values	E-Ld cohort	Ld cohort		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	374	374		
Units: Months				
median (confidence interval 95%)	31.38 (26.18 to 36.80)	29.47 (23.49 to 34.30)		

Statistical analyses

Statistical analysis title	Statistical Analysis for PFS
Comparison groups	E-Ld cohort v Ld cohort
Number of subjects included in analysis	748
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.4358
Method	Stratified Log Rank

Statistical analysis title	Statistical Analysis of PFS
Comparison groups	E-Ld cohort v Ld cohort
Number of subjects included in analysis	748
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Hazard ratio (HR)
Point estimate	0.93
Confidence interval	
level	95.71 %
sides	2-sided
lower limit	0.77
upper limit	1.12

Secondary: Objective Response Rate (ORR)

End point title	Objective Response Rate (ORR)
End point description:	
ORR is defined as the percentage of participants with objective response among all randomized subjects. Participants with an objective response are those participants experiencing a partial response (PR) or better, based on Independent Review Committee (IRC) assessment, as per EBMT criteria.	
End point type	Secondary
End point timeframe:	
From randomization to primary completion date (approximately 8 years)	

End point values	E-Ld cohort	Ld cohort		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	374	374		
Units: Percent of Participants				
number (confidence interval 95%)	82.9 (78.7 to 86.6)	79.4 (75.0 to 83.4)		

Statistical analyses

Statistical analysis title	Statistical Analysis for ORR
Comparison groups	E-Ld cohort v Ld cohort
Number of subjects included in analysis	748
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.2232
Method	CMH ESTIMATE OF COMMON ODDS RATIO
Parameter estimate	CMH ESTIMATE OF COMMON ODDS RATIO
Point estimate	1.26
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.87
upper limit	1.82

Secondary: Overall Survival (OS)

End point title	Overall Survival (OS)
End point description:	
Survival is defined as the time from randomization to the date of death. A participant who did not die had his or her survival duration censored at the date of last contact ('last known date alive').	
End point type	Secondary
End point timeframe:	
From randomization to the date of death (up to 8 years)	

End point values	E-Ld cohort	Ld cohort		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	374	374		
Units: Months				
median (confidence interval 95%)	60.42 (52.76 to 67.35)	57.56 (48.95 to 66.56)		

Statistical analyses

Statistical analysis title	Statistical Analysis for OS
Comparison groups	E-Ld cohort v Ld cohort
Number of subjects included in analysis	748
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.8932
Method	Stratified log rank test
Parameter estimate	Hazard ratio (HR)
Point estimate	0.99

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.82
upper limit	1.19

Secondary: Mean Change from Baseline of Pain Severity Score and Pain Interference Score

End point title	Mean Change from Baseline of Pain Severity Score and Pain Interference Score
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End point description:

Pain severity (sensory dimension) and pain interference (reactive dimension, assessing the degree to which pain interferes with function) are measured using the Brief Pain Inventory- Short Form (BPI-SF). BPI-SF numeric rating scale goes from 0 (No pain) to 10 (Pain as bad as you can imagine).

End point type	Secondary
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End point timeframe:

From Baseline to End of Treatment (approximately 8 years)

End point values	E-Ld cohort	Ld cohort		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	374	374		
Units: Rating score				
arithmetic mean (standard deviation)				
Pain Severity	0.02 (± 2.645)	-0.25 (± 2.721)		
Pain Interference	0.33 (± 3.077)	-0.18 (± 3.082)		

Statistical analyses

No statistical analyses for this end point

Secondary: Progression Free Survival (PFS) Rate at Specific Time-points

End point title	Progression Free Survival (PFS) Rate at Specific Time-points
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End point description:

PFS rate is defined as the proportion of participants experiencing PFS at the defined time-points.

End point type	Secondary
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End point timeframe:

From randomization to the specified time-point (up to 5 years)

End point values	E-Ld cohort	Ld cohort		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	374	374		
Units: Percent of participants				
number (confidence interval 95%)				
1 year	0.77 (0.72 to 0.81)	0.76 (0.71 to 0.80)		
2 year	0.59 (0.53 to 0.64)	0.55 (0.49 to 0.60)		
3 year	0.46 (0.40 to 0.51)	0.41 (0.35 to 0.46)		
4 year	0.36 (0.31 to 0.41)	0.33 (0.28 to 0.38)		
5 year	0.26 (0.21 to 0.32)	0.25 (0.20 to 0.30)		

Statistical analyses

Statistical analysis title	Statistical Analysis for PFS
Statistical analysis description:	
Statistical Analysis for PFS at specific time points	
Comparison groups	E-Ld cohort v Ld cohort
Number of subjects included in analysis	748
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.4358
Method	Hazard Ratio
Parameter estimate	Hazard ratio (HR)
Point estimate	0.93
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.78
upper limit	1.12

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From first dose to 60 days after last dose (up to 93.3 months)

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
Dictionary version	MedDRA24.1

Reporting groups

Reporting group title	Ld Cohort
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Reporting group description:

Participants receiving a combination of
Lenalidomide (L)
Dexamethasone (d)
in a 28 day cycle

Reporting group title	E-Ld Cohort
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Reporting group description:

Participants receiving a combination of
Elotuzumab (E)
Lenalidomide (L)
Dexamethasone (d)
in a 28 day cycle

Serious adverse events	Ld Cohort	E-Ld Cohort	
Total subjects affected by serious adverse events			
subjects affected / exposed	279 / 371 (75.20%)	293 / 371 (78.98%)	
number of deaths (all causes)	232	240	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute lymphocytic leukaemia			
subjects affected / exposed	2 / 371 (0.54%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adenocarcinoma metastatic			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Adenocarcinoma pancreas			

subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Angiosarcoma			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Atypical fibroxanthoma			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Basal cell carcinoma			
subjects affected / exposed	10 / 371 (2.70%)	10 / 371 (2.70%)	
occurrences causally related to treatment / all	6 / 11	6 / 14	
deaths causally related to treatment / all	0 / 0	0 / 0	
Basosquamous carcinoma			
subjects affected / exposed	1 / 371 (0.27%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder neoplasm			
subjects affected / exposed	1 / 371 (0.27%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bowen's disease			
subjects affected / exposed	2 / 371 (0.54%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholangiocarcinoma			
subjects affected / exposed	1 / 371 (0.27%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Colon cancer			

subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colon cancer metastatic			
subjects affected / exposed	1 / 371 (0.27%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Hepatic cancer			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric cancer			
subjects affected / exposed	1 / 371 (0.27%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Hepatocellular carcinoma			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intraductal proliferative breast lesion			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Keratoacanthoma			
subjects affected / exposed	1 / 371 (0.27%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laryngeal cancer			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lip squamous cell carcinoma			

subjects affected / exposed	1 / 371 (0.27%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laryngeal squamous cell carcinoma			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung adenocarcinoma			
subjects affected / exposed	2 / 371 (0.54%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malignant melanoma			
subjects affected / exposed	1 / 371 (0.27%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Malignant melanoma in situ			
subjects affected / exposed	2 / 371 (0.54%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malignant neoplasm progression			
subjects affected / exposed	1 / 371 (0.27%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Myelodysplastic syndrome			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nasal cavity cancer			
subjects affected / exposed	1 / 371 (0.27%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatic carcinoma			

subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Papilloma			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Plasma cell leukaemia			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Plasma cell myeloma			
subjects affected / exposed	3 / 371 (0.81%)	5 / 371 (1.35%)	
occurrences causally related to treatment / all	0 / 3	0 / 5	
deaths causally related to treatment / all	0 / 2	0 / 3	
Plasmacytoma			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostate cancer			
subjects affected / exposed	0 / 371 (0.00%)	5 / 371 (1.35%)	
occurrences causally related to treatment / all	0 / 0	1 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal cancer			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectosigmoid cancer			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Refractory anaemia with ringed sideroblasts			

subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sebacous carcinoma			
subjects affected / exposed	1 / 371 (0.27%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spindle cell sarcoma			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous cell carcinoma			
subjects affected / exposed	7 / 371 (1.89%)	13 / 371 (3.50%)	
occurrences causally related to treatment / all	5 / 9	6 / 21	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous cell carcinoma of skin			
subjects affected / exposed	7 / 371 (1.89%)	9 / 371 (2.43%)	
occurrences causally related to treatment / all	3 / 14	4 / 12	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous cell carcinoma of head and neck			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transitional cell carcinoma			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Squamous cell carcinoma of the oral cavity			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			

Aortic aneurysm			
subjects affected / exposed	2 / 371 (0.54%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Arteriosclerosis			
subjects affected / exposed	1 / 371 (0.27%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Circulatory collapse			
subjects affected / exposed	1 / 371 (0.27%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Deep vein thrombosis			
subjects affected / exposed	10 / 371 (2.70%)	9 / 371 (2.43%)	
occurrences causally related to treatment / all	8 / 10	7 / 9	
deaths causally related to treatment / all	0 / 0	0 / 0	
Embolism			
subjects affected / exposed	0 / 371 (0.00%)	3 / 371 (0.81%)	
occurrences causally related to treatment / all	0 / 0	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 2	
Embolism venous			
subjects affected / exposed	1 / 371 (0.27%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematoma			
subjects affected / exposed	1 / 371 (0.27%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertension			
subjects affected / exposed	2 / 371 (0.54%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypotension			

subjects affected / exposed	2 / 371 (0.54%)	7 / 371 (1.89%)	
occurrences causally related to treatment / all	0 / 2	1 / 7	
deaths causally related to treatment / all	0 / 1	0 / 0	
Hypovolaemic shock			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Malignant hypertension			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Orthostatic hypotension			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral artery thrombosis			
subjects affected / exposed	1 / 371 (0.27%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral ischaemia			
subjects affected / exposed	1 / 371 (0.27%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Superficial vein thrombosis			
subjects affected / exposed	1 / 371 (0.27%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombophlebitis			
subjects affected / exposed	0 / 371 (0.00%)	2 / 371 (0.54%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombosis			

subjects affected / exposed	1 / 371 (0.27%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Venous thrombosis			
subjects affected / exposed	1 / 371 (0.27%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Adverse drug reaction			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Asthenia			
subjects affected / exposed	6 / 371 (1.62%)	3 / 371 (0.81%)	
occurrences causally related to treatment / all	1 / 6	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest pain			
subjects affected / exposed	4 / 371 (1.08%)	2 / 371 (0.54%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Complication associated with device			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Death			
subjects affected / exposed	3 / 371 (0.81%)	2 / 371 (0.54%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 3	0 / 2	
Disease progression			
subjects affected / exposed	5 / 371 (1.35%)	8 / 371 (2.16%)	
occurrences causally related to treatment / all	0 / 5	0 / 8	
deaths causally related to treatment / all	0 / 5	0 / 8	
Fat necrosis			

subjects affected / exposed	1 / 371 (0.27%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General physical health deterioration			
subjects affected / exposed	5 / 371 (1.35%)	3 / 371 (0.81%)	
occurrences causally related to treatment / all	1 / 5	1 / 3	
deaths causally related to treatment / all	0 / 2	0 / 1	
Fatigue			
subjects affected / exposed	2 / 371 (0.54%)	2 / 371 (0.54%)	
occurrences causally related to treatment / all	0 / 2	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inflammation			
subjects affected / exposed	0 / 371 (0.00%)	2 / 371 (0.54%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malaise			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple organ dysfunction syndrome			
subjects affected / exposed	1 / 371 (0.27%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Non-cardiac chest pain			
subjects affected / exposed	3 / 371 (0.81%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oedema peripheral			
subjects affected / exposed	4 / 371 (1.08%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	2 / 4	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oedema			

subjects affected / exposed	1 / 371 (0.27%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain			
subjects affected / exposed	3 / 371 (0.81%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Performance status decreased			
subjects affected / exposed	1 / 371 (0.27%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	7 / 371 (1.89%)	19 / 371 (5.12%)	
occurrences causally related to treatment / all	1 / 7	11 / 21	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sudden cardiac death			
subjects affected / exposed	1 / 371 (0.27%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Sudden death			
subjects affected / exposed	1 / 371 (0.27%)	2 / 371 (0.54%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 2	
Systemic inflammatory response syndrome			
subjects affected / exposed	1 / 371 (0.27%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	1 / 371 (0.27%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypersensitivity			

subjects affected / exposed	0 / 371 (0.00%)	2 / 371 (0.54%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Endometrial hyperplasia			
subjects affected / exposed	1 / 371 (0.27%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine prolapse			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Acute pulmonary oedema			
subjects affected / exposed	0 / 371 (0.00%)	2 / 371 (0.54%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Acute respiratory failure			
subjects affected / exposed	0 / 371 (0.00%)	3 / 371 (0.81%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 1	
Bronchiectasis			
subjects affected / exposed	1 / 371 (0.27%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 14	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchopneumopathy			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Bronchospasm			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Chronic obstructive pulmonary disease			
subjects affected / exposed	7 / 371 (1.89%)	3 / 371 (0.81%)	
occurrences causally related to treatment / all	3 / 10	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cough			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			
subjects affected / exposed	8 / 371 (2.16%)	13 / 371 (3.50%)	
occurrences causally related to treatment / all	1 / 8	3 / 15	
deaths causally related to treatment / all	0 / 1	0 / 0	
Epistaxis			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoxia			
subjects affected / exposed	2 / 371 (0.54%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	1 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Interstitial lung disease			
subjects affected / exposed	3 / 371 (0.81%)	3 / 371 (0.81%)	
occurrences causally related to treatment / all	0 / 3	2 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			
subjects affected / exposed	3 / 371 (0.81%)	5 / 371 (1.35%)	
occurrences causally related to treatment / all	1 / 3	0 / 7	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pleuritic pain			
subjects affected / exposed	1 / 371 (0.27%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonitis			

subjects affected / exposed	4 / 371 (1.08%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	1 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumothorax			
subjects affected / exposed	1 / 371 (0.27%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary congestion			
subjects affected / exposed	1 / 371 (0.27%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	15 / 371 (4.04%)	12 / 371 (3.23%)	
occurrences causally related to treatment / all	14 / 15	9 / 13	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary oedema			
subjects affected / exposed	4 / 371 (1.08%)	3 / 371 (0.81%)	
occurrences causally related to treatment / all	1 / 4	2 / 3	
deaths causally related to treatment / all	0 / 1	0 / 1	
Respiratory depression			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Respiratory disorder			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory distress			
subjects affected / exposed	1 / 371 (0.27%)	2 / 371 (0.54%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Respiratory failure			

subjects affected / exposed	3 / 371 (0.81%)	4 / 371 (1.08%)	
occurrences causally related to treatment / all	0 / 3	0 / 4	
deaths causally related to treatment / all	0 / 1	0 / 1	
Restrictive pulmonary disease			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinus disorder			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vocal cord disorder			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	2 / 371 (0.54%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Completed suicide			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Confusional state			
subjects affected / exposed	5 / 371 (1.35%)	5 / 371 (1.35%)	
occurrences causally related to treatment / all	0 / 5	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Delirium			
subjects affected / exposed	0 / 371 (0.00%)	2 / 371 (0.54%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Delusional disorder, unspecified type			

subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Depression			
subjects affected / exposed	0 / 371 (0.00%)	2 / 371 (0.54%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mental status changes			
subjects affected / exposed	1 / 371 (0.27%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychotic disorder			
subjects affected / exposed	1 / 371 (0.27%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Product issues			
Device dislocation			
subjects affected / exposed	0 / 371 (0.00%)	2 / 371 (0.54%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	4 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacterial test positive			
subjects affected / exposed	1 / 371 (0.27%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	1 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

Blood creatinine increased			
subjects affected / exposed	2 / 371 (0.54%)	2 / 371 (0.54%)	
occurrences causally related to treatment / all	1 / 2	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
C-reactive protein increased			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemoglobin decreased			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic enzyme increased			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza A virus test positive			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza B virus test positive			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liver function test abnormal			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory syncytial virus test positive			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respirovirus test positive			

subjects affected / exposed	1 / 371 (0.27%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transaminases increased			
subjects affected / exposed	2 / 371 (0.54%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral test positive			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Weight decreased			
subjects affected / exposed	1 / 371 (0.27%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Accidental overdose			
subjects affected / exposed	1 / 371 (0.27%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Combined tibia-fibula fracture			
subjects affected / exposed	1 / 371 (0.27%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Comminuted fracture			
subjects affected / exposed	1 / 371 (0.27%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Extradural haematoma			
subjects affected / exposed	1 / 371 (0.27%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fall			

subjects affected / exposed	3 / 371 (0.81%)	3 / 371 (0.81%)	
occurrences causally related to treatment / all	0 / 4	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femoral neck fracture			
subjects affected / exposed	2 / 371 (0.54%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femur fracture			
subjects affected / exposed	8 / 371 (2.16%)	4 / 371 (1.08%)	
occurrences causally related to treatment / all	0 / 9	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fibula fracture			
subjects affected / exposed	2 / 371 (0.54%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fracture			
subjects affected / exposed	0 / 371 (0.00%)	3 / 371 (0.81%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Head injury			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hip fracture			
subjects affected / exposed	4 / 371 (1.08%)	5 / 371 (1.35%)	
occurrences causally related to treatment / all	0 / 4	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Humerus fracture			
subjects affected / exposed	1 / 371 (0.27%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Joint injury			

subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infusion related reaction			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lumbar vertebral fracture			
subjects affected / exposed	1 / 371 (0.27%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Medication error			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pelvic fracture			
subjects affected / exposed	2 / 371 (0.54%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Overdose			
subjects affected / exposed	0 / 371 (0.00%)	2 / 371 (0.54%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural complication			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Rib fracture			
subjects affected / exposed	4 / 371 (1.08%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Shunt malfunction			

subjects affected / exposed	1 / 371 (0.27%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin laceration			
subjects affected / exposed	1 / 371 (0.27%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal compression fracture			
subjects affected / exposed	4 / 371 (1.08%)	2 / 371 (0.54%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal fracture			
subjects affected / exposed	3 / 371 (0.81%)	2 / 371 (0.54%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stress fracture			
subjects affected / exposed	1 / 371 (0.27%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subdural haematoma			
subjects affected / exposed	2 / 371 (0.54%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Thoracic vertebral fracture			
subjects affected / exposed	1 / 371 (0.27%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tibia fracture			
subjects affected / exposed	2 / 371 (0.54%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Traumatic fracture			

subjects affected / exposed	2 / 371 (0.54%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wrist fracture			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper limb fracture			
subjects affected / exposed	1 / 371 (0.27%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congenital, familial and genetic disorders			
Corneal dystrophy			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute coronary syndrome			
subjects affected / exposed	2 / 371 (0.54%)	2 / 371 (0.54%)	
occurrences causally related to treatment / all	1 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute myocardial infarction			
subjects affected / exposed	0 / 371 (0.00%)	7 / 371 (1.89%)	
occurrences causally related to treatment / all	0 / 0	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina pectoris			
subjects affected / exposed	0 / 371 (0.00%)	2 / 371 (0.54%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina unstable			
subjects affected / exposed	1 / 371 (0.27%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Aortic valve calcification			
subjects affected / exposed	1 / 371 (0.27%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic valve incompetence			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Arrhythmia			
subjects affected / exposed	2 / 371 (0.54%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 2	1 / 1	
deaths causally related to treatment / all	0 / 1	1 / 1	
Atrial fibrillation			
subjects affected / exposed	12 / 371 (3.23%)	22 / 371 (5.93%)	
occurrences causally related to treatment / all	4 / 14	3 / 26	
deaths causally related to treatment / all	0 / 0	1 / 2	
Atrial flutter			
subjects affected / exposed	3 / 371 (0.81%)	4 / 371 (1.08%)	
occurrences causally related to treatment / all	1 / 3	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial tachycardia			
subjects affected / exposed	2 / 371 (0.54%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial thrombosis			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrioventricular block			
subjects affected / exposed	1 / 371 (0.27%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bradycardia			

subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac arrest			
subjects affected / exposed	6 / 371 (1.62%)	7 / 371 (1.89%)	
occurrences causally related to treatment / all	0 / 6	0 / 7	
deaths causally related to treatment / all	0 / 6	0 / 6	
Cardiac failure			
subjects affected / exposed	7 / 371 (1.89%)	13 / 371 (3.50%)	
occurrences causally related to treatment / all	0 / 7	1 / 16	
deaths causally related to treatment / all	0 / 2	0 / 4	
Cardiac failure acute			
subjects affected / exposed	1 / 371 (0.27%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cardiac failure chronic			
subjects affected / exposed	1 / 371 (0.27%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	2 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure congestive			
subjects affected / exposed	4 / 371 (1.08%)	4 / 371 (1.08%)	
occurrences causally related to treatment / all	2 / 4	2 / 6	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cardiac septal hypertrophy			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac ventricular thrombosis			
subjects affected / exposed	1 / 371 (0.27%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiogenic shock			

subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cardio-respiratory arrest			
subjects affected / exposed	1 / 371 (0.27%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Cardiomyopathy			
subjects affected / exposed	1 / 371 (0.27%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiopulmonary failure			
subjects affected / exposed	1 / 371 (0.27%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cardiovascular disorder			
subjects affected / exposed	0 / 371 (0.00%)	2 / 371 (0.54%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 2	
Congestive cardiomyopathy			
subjects affected / exposed	1 / 371 (0.27%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery disease			
subjects affected / exposed	1 / 371 (0.27%)	2 / 371 (0.54%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Left ventricular dysfunction			
subjects affected / exposed	2 / 371 (0.54%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mitral valve incompetence			

subjects affected / exposed	0 / 371 (0.00%)	2 / 371 (0.54%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Myocardial infarction			
subjects affected / exposed	5 / 371 (1.35%)	6 / 371 (1.62%)	
occurrences causally related to treatment / all	1 / 5	0 / 6	
deaths causally related to treatment / all	0 / 1	0 / 2	
Pericarditis			
subjects affected / exposed	1 / 371 (0.27%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial ischaemia			
subjects affected / exposed	1 / 371 (0.27%)	2 / 371 (0.54%)	
occurrences causally related to treatment / all	0 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prinzmetal angina			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinus arrest			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinus node dysfunction			
subjects affected / exposed	1 / 371 (0.27%)	3 / 371 (0.81%)	
occurrences causally related to treatment / all	0 / 1	2 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinus tachycardia			
subjects affected / exposed	1 / 371 (0.27%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Systolic dysfunction			

subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Supraventricular tachycardia			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tachycardia			
subjects affected / exposed	0 / 371 (0.00%)	3 / 371 (0.81%)	
occurrences causally related to treatment / all	0 / 0	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Torsade de pointes			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular arrhythmia			
subjects affected / exposed	1 / 371 (0.27%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Ataxia			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carotid artery stenosis			
subjects affected / exposed	1 / 371 (0.27%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebellar haemorrhage			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral haemorrhage			

subjects affected / exposed	3 / 371 (0.81%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 2	0 / 0	
Cerebral infarction			
subjects affected / exposed	2 / 371 (0.54%)	2 / 371 (0.54%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral ischaemia			
subjects affected / exposed	2 / 371 (0.54%)	3 / 371 (0.81%)	
occurrences causally related to treatment / all	0 / 2	2 / 3	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cerebrovascular accident			
subjects affected / exposed	7 / 371 (1.89%)	8 / 371 (2.16%)	
occurrences causally related to treatment / all	5 / 8	3 / 8	
deaths causally related to treatment / all	0 / 1	0 / 1	
Coma			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cognitive disorder			
subjects affected / exposed	1 / 371 (0.27%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dementia			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Depressed level of consciousness			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dizziness			

subjects affected / exposed	1 / 371 (0.27%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dizziness postural			
subjects affected / exposed	1 / 371 (0.27%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Encephalopathy			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysarthria			
subjects affected / exposed	0 / 371 (0.00%)	2 / 371 (0.54%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Generalised tonic-clonic seizure			
subjects affected / exposed	1 / 371 (0.27%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Guillain-Barre syndrome			
subjects affected / exposed	1 / 371 (0.27%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhage intracranial			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhagic cerebral infarction			
subjects affected / exposed	1 / 371 (0.27%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhagic stroke			

subjects affected / exposed	1 / 371 (0.27%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Headache			
subjects affected / exposed	1 / 371 (0.27%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intracranial aneurysm			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intracranial haematoma			
subjects affected / exposed	1 / 371 (0.27%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic cerebral infarction			
subjects affected / exposed	1 / 371 (0.27%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic stroke			
subjects affected / exposed	1 / 371 (0.27%)	4 / 371 (1.08%)	
occurrences causally related to treatment / all	0 / 1	2 / 4	
deaths causally related to treatment / all	0 / 0	0 / 1	
Lethargy			
subjects affected / exposed	1 / 371 (0.27%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Loss of consciousness			
subjects affected / exposed	1 / 371 (0.27%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Memory impairment			

subjects affected / exposed	1 / 371 (0.27%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolic encephalopathy			
subjects affected / exposed	1 / 371 (0.27%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Migraine			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myelopathy			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Normal pressure hydrocephalus			
subjects affected / exposed	1 / 371 (0.27%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Presyncope			
subjects affected / exposed	0 / 371 (0.00%)	2 / 371 (0.54%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sciatica			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal cord compression			
subjects affected / exposed	1 / 371 (0.27%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Somnolence			

subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subarachnoid haemorrhage			
subjects affected / exposed	0 / 371 (0.00%)	2 / 371 (0.54%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Syncope			
subjects affected / exposed	5 / 371 (1.35%)	7 / 371 (1.89%)	
occurrences causally related to treatment / all	0 / 5	2 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient aphasia			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient ischaemic attack			
subjects affected / exposed	4 / 371 (1.08%)	6 / 371 (1.62%)	
occurrences causally related to treatment / all	0 / 4	1 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Agranulocytosis			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anaemia			
subjects affected / exposed	12 / 371 (3.23%)	12 / 371 (3.23%)	
occurrences causally related to treatment / all	4 / 17	5 / 16	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile neutropenia			
subjects affected / exposed	3 / 371 (0.81%)	5 / 371 (1.35%)	
occurrences causally related to treatment / all	1 / 3	3 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemolysis			

subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemolytic anaemia			
subjects affected / exposed	1 / 371 (0.27%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenia			
subjects affected / exposed	1 / 371 (0.27%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancytopenia			
subjects affected / exposed	0 / 371 (0.00%)	4 / 371 (1.08%)	
occurrences causally related to treatment / all	0 / 0	1 / 4	
deaths causally related to treatment / all	0 / 0	0 / 1	
Plasmacytosis			
subjects affected / exposed	1 / 371 (0.27%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Thrombocytopenia			
subjects affected / exposed	2 / 371 (0.54%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	2 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Sudden hearing loss			
subjects affected / exposed	1 / 371 (0.27%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vertigo			
subjects affected / exposed	1 / 371 (0.27%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			

Blindness transient			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cataract			
subjects affected / exposed	9 / 371 (2.43%)	10 / 371 (2.70%)	
occurrences causally related to treatment / all	8 / 13	6 / 13	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cataract cortical			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epiretinal membrane			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Optic ischaemic neuropathy			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retinal detachment			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	2 / 371 (0.54%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	1 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain lower			
subjects affected / exposed	1 / 371 (0.27%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain upper			

subjects affected / exposed	1 / 371 (0.27%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal haemorrhage			
subjects affected / exposed	1 / 371 (0.27%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anorectal varices haemorrhage			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis			
subjects affected / exposed	1 / 371 (0.27%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis ulcerative			
subjects affected / exposed	1 / 371 (0.27%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Constipation			
subjects affected / exposed	2 / 371 (0.54%)	3 / 371 (0.81%)	
occurrences causally related to treatment / all	1 / 2	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diaphragmatic hernia			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	10 / 371 (2.70%)	9 / 371 (2.43%)	
occurrences causally related to treatment / all	3 / 11	2 / 10	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulum intestinal			

subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenal ulcer			
subjects affected / exposed	1 / 371 (0.27%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enteritis			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterovesical fistula			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femoral hernia			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastritis			
subjects affected / exposed	0 / 371 (0.00%)	4 / 371 (1.08%)	
occurrences causally related to treatment / all	0 / 0	1 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal haemorrhage			
subjects affected / exposed	1 / 371 (0.27%)	2 / 371 (0.54%)	
occurrences causally related to treatment / all	1 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hiatus hernia			
subjects affected / exposed	1 / 371 (0.27%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileus			

subjects affected / exposed	2 / 371 (0.54%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	1 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Incarcerated inguinal hernia			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Incarcerated umbilical hernia			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inguinal hernia			
subjects affected / exposed	2 / 371 (0.54%)	3 / 371 (0.81%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inguinal hernia strangulated			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal infarction			
subjects affected / exposed	1 / 371 (0.27%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal obstruction			
subjects affected / exposed	2 / 371 (0.54%)	4 / 371 (1.08%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal perforation			
subjects affected / exposed	2 / 371 (0.54%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestine polyp			

subjects affected / exposed	1 / 371 (0.27%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower gastrointestinal haemorrhage			
subjects affected / exposed	1 / 371 (0.27%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Melaena			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			
subjects affected / exposed	3 / 371 (0.81%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	2 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Odynophagia			
subjects affected / exposed	1 / 371 (0.27%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal ulcer			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophagitis			
subjects affected / exposed	1 / 371 (0.27%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oroantral fistula			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis			

subjects affected / exposed	3 / 371 (0.81%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis acute			
subjects affected / exposed	1 / 371 (0.27%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumatosis intestinalis			
subjects affected / exposed	1 / 371 (0.27%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal haemorrhage			
subjects affected / exposed	2 / 371 (0.54%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal obstruction			
subjects affected / exposed	1 / 371 (0.27%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Umbilical hernia			
subjects affected / exposed	1 / 371 (0.27%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Varices oesophageal			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	1 / 371 (0.27%)	3 / 371 (0.81%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Bile duct stone			

subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Biliary obstruction			
subjects affected / exposed	1 / 371 (0.27%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis			
subjects affected / exposed	1 / 371 (0.27%)	2 / 371 (0.54%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis acute			
subjects affected / exposed	0 / 371 (0.00%)	2 / 371 (0.54%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis chronic			
subjects affected / exposed	1 / 371 (0.27%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholelithiasis			
subjects affected / exposed	1 / 371 (0.27%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gallbladder rupture			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hydrocholecystis			
subjects affected / exposed	1 / 371 (0.27%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Jaundice			

subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Actinic keratosis			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angioedema			
subjects affected / exposed	1 / 371 (0.27%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cold sweat			
subjects affected / exposed	1 / 371 (0.27%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cutaneous vasculitis			
subjects affected / exposed	1 / 371 (0.27%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dermatitis bullous			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dermatitis exfoliative generalised			
subjects affected / exposed	1 / 371 (0.27%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic foot			
subjects affected / exposed	1 / 371 (0.27%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Erythema			

subjects affected / exposed	1 / 371 (0.27%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Exfoliative rash			
subjects affected / exposed	2 / 371 (0.54%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Purpura			
subjects affected / exposed	1 / 371 (0.27%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rash			
subjects affected / exposed	1 / 371 (0.27%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rash maculo-papular			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin ulcer			
subjects affected / exposed	1 / 371 (0.27%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stasis dermatitis			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subcutaneous emphysema			
subjects affected / exposed	1 / 371 (0.27%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stevens-Johnson syndrome			

subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	20 / 371 (5.39%)	20 / 371 (5.39%)	
occurrences causally related to treatment / all	4 / 21	4 / 20	
deaths causally related to treatment / all	0 / 1	0 / 2	
Calculus urinary			
subjects affected / exposed	1 / 371 (0.27%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic kidney disease			
subjects affected / exposed	0 / 371 (0.00%)	2 / 371 (0.54%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
End stage renal disease			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myeloma cast nephropathy			
subjects affected / exposed	1 / 371 (0.27%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Haematuria			
subjects affected / exposed	2 / 371 (0.54%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal failure			
subjects affected / exposed	7 / 371 (1.89%)	10 / 371 (2.70%)	
occurrences causally related to treatment / all	2 / 7	5 / 10	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephrolithiasis			

subjects affected / exposed	2 / 371 (0.54%)	2 / 371 (0.54%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal impairment			
subjects affected / exposed	3 / 371 (0.81%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	1 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal injury			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal tubular necrosis			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary retention			
subjects affected / exposed	0 / 371 (0.00%)	2 / 371 (0.54%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract disorder			
subjects affected / exposed	1 / 371 (0.27%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Adrenal insufficiency			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 371 (0.54%)	2 / 371 (0.54%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

Arthritis			
subjects affected / exposed	1 / 371 (0.27%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthritis reactive			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Back pain			
subjects affected / exposed	9 / 371 (2.43%)	11 / 371 (2.96%)	
occurrences causally related to treatment / all	0 / 11	0 / 14	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bone pain			
subjects affected / exposed	4 / 371 (1.08%)	3 / 371 (0.81%)	
occurrences causally related to treatment / all	0 / 4	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bursitis			
subjects affected / exposed	1 / 371 (0.27%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chondrocalcinosis			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chondrocalcinosis pyrophosphate			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral disc protrusion			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Flank pain			

subjects affected / exposed	1 / 371 (0.27%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscle contracture			
subjects affected / exposed	1 / 371 (0.27%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Joint hyperextension			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscular weakness			
subjects affected / exposed	1 / 371 (0.27%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal chest pain			
subjects affected / exposed	1 / 371 (0.27%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal disorder			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal pain			
subjects affected / exposed	1 / 371 (0.27%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteitis			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoarthritis			

subjects affected / exposed	0 / 371 (0.00%)	3 / 371 (0.81%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteonecrosis			
subjects affected / exposed	0 / 371 (0.00%)	2 / 371 (0.54%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteonecrosis of jaw			
subjects affected / exposed	2 / 371 (0.54%)	3 / 371 (0.81%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain in extremity			
subjects affected / exposed	2 / 371 (0.54%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pathological fracture			
subjects affected / exposed	1 / 371 (0.27%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal pain			
subjects affected / exposed	1 / 371 (0.27%)	3 / 371 (0.81%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal stenosis			
subjects affected / exposed	1 / 371 (0.27%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Abdominal abscess			
subjects affected / exposed	1 / 371 (0.27%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abscess limb			

subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abscess			
subjects affected / exposed	1 / 371 (0.27%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atypical pneumonia			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Bacteraemia			
subjects affected / exposed	1 / 371 (0.27%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacterial prostatitis			
subjects affected / exposed	1 / 371 (0.27%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Biliary sepsis			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	6 / 371 (1.62%)	18 / 371 (4.85%)	
occurrences causally related to treatment / all	1 / 6	6 / 20	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bursitis infective			

subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	8 / 371 (2.16%)	9 / 371 (2.43%)	
occurrences causally related to treatment / all	1 / 9	0 / 9	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis orbital			
subjects affected / exposed	1 / 371 (0.27%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Central nervous system infection			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridial sepsis			
subjects affected / exposed	1 / 371 (0.27%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium colitis			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Clostridium difficile colitis			
subjects affected / exposed	1 / 371 (0.27%)	2 / 371 (0.54%)	
occurrences causally related to treatment / all	0 / 2	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium difficile infection			
subjects affected / exposed	1 / 371 (0.27%)	2 / 371 (0.54%)	
occurrences causally related to treatment / all	0 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dacryocystitis			

subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device related infection			
subjects affected / exposed	1 / 371 (0.27%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulitis			
subjects affected / exposed	3 / 371 (0.81%)	5 / 371 (1.35%)	
occurrences causally related to treatment / all	0 / 3	4 / 10	
deaths causally related to treatment / all	0 / 0	0 / 0	
Erysipelas			
subjects affected / exposed	1 / 371 (0.27%)	2 / 371 (0.54%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia bacteraemia			
subjects affected / exposed	2 / 371 (0.54%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia infection			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia urinary tract infection			
subjects affected / exposed	1 / 371 (0.27%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile infection			
subjects affected / exposed	0 / 371 (0.00%)	2 / 371 (0.54%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			

subjects affected / exposed	2 / 371 (0.54%)	8 / 371 (2.16%)	
occurrences causally related to treatment / all	0 / 2	2 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis clostridial			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis salmonella			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal infection			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis viral			
subjects affected / exposed	1 / 371 (0.27%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
H1N1 influenza			
subjects affected / exposed	1 / 371 (0.27%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis E			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes zoster			
subjects affected / exposed	2 / 371 (0.54%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes zoster disseminated			

subjects affected / exposed	1 / 371 (0.27%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infected cyst			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infection			
subjects affected / exposed	1 / 371 (0.27%)	4 / 371 (1.08%)	
occurrences causally related to treatment / all	0 / 1	2 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infectious pleural effusion			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Influenza			
subjects affected / exposed	6 / 371 (1.62%)	7 / 371 (1.89%)	
occurrences causally related to treatment / all	1 / 7	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral discitis			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestine infection			
subjects affected / exposed	1 / 371 (0.27%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Leishmaniasis			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liver abscess			

subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Localised infection			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningitis listeria			
subjects affected / exposed	1 / 371 (0.27%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Lower respiratory tract infection			
subjects affected / exposed	8 / 371 (2.16%)	9 / 371 (2.43%)	
occurrences causally related to treatment / all	4 / 8	1 / 10	
deaths causally related to treatment / all	0 / 1	0 / 0	
Metapneumovirus bronchiolitis			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metapneumovirus infection			
subjects affected / exposed	1 / 371 (0.27%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenic sepsis			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Orchitis			
subjects affected / exposed	1 / 371 (0.27%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Perirectal abscess			

subjects affected / exposed	1 / 371 (0.27%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritonitis			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pharyngitis			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Plague			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural infection			
subjects affected / exposed	1 / 371 (0.27%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pneumococcal sepsis			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumocystis jirovecii pneumonia			
subjects affected / exposed	0 / 371 (0.00%)	2 / 371 (0.54%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pneumonia			
subjects affected / exposed	48 / 371 (12.94%)	60 / 371 (16.17%)	
occurrences causally related to treatment / all	11 / 58	21 / 80	
deaths causally related to treatment / all	1 / 5	2 / 10	
Pneumonia aspiration			

subjects affected / exposed	0 / 371 (0.00%)	5 / 371 (1.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 2	
Pneumonia bacterial			
subjects affected / exposed	1 / 371 (0.27%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia cytomegaloviral			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia fungal			
subjects affected / exposed	0 / 371 (0.00%)	2 / 371 (0.54%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia influenzal			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia legionella			
subjects affected / exposed	1 / 371 (0.27%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pneumonia staphylococcal			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Pneumonia streptococcal			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia viral			

subjects affected / exposed	1 / 371 (0.27%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Progressive multifocal leukoencephalopathy			
subjects affected / exposed	1 / 371 (0.27%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Pseudomembranous colitis			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis			
subjects affected / exposed	2 / 371 (0.54%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyoderma			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory syncytial virus infection			
subjects affected / exposed	1 / 371 (0.27%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory tract infection			
subjects affected / exposed	3 / 371 (0.81%)	8 / 371 (2.16%)	
occurrences causally related to treatment / all	2 / 5	2 / 9	
deaths causally related to treatment / all	0 / 0	0 / 1	
Sepsis			
subjects affected / exposed	6 / 371 (1.62%)	15 / 371 (4.04%)	
occurrences causally related to treatment / all	3 / 6	1 / 15	
deaths causally related to treatment / all	0 / 1	0 / 5	
Septic shock			

subjects affected / exposed	6 / 371 (1.62%)	4 / 371 (1.08%)	
occurrences causally related to treatment / all	2 / 6	0 / 4	
deaths causally related to treatment / all	2 / 5	0 / 4	
Staphylococcal infection			
subjects affected / exposed	0 / 371 (0.00%)	2 / 371 (0.54%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal sepsis			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subcutaneous abscess			
subjects affected / exposed	1 / 371 (0.27%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection			
subjects affected / exposed	4 / 371 (1.08%)	5 / 371 (1.35%)	
occurrences causally related to treatment / all	1 / 4	1 / 5	
deaths causally related to treatment / all	0 / 1	0 / 0	
Urinary tract infection			
subjects affected / exposed	11 / 371 (2.96%)	15 / 371 (4.04%)	
occurrences causally related to treatment / all	3 / 13	2 / 19	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection bacterial			
subjects affected / exposed	1 / 371 (0.27%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection enterococcal			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urosepsis			

subjects affected / exposed	5 / 371 (1.35%)	5 / 371 (1.35%)	
occurrences causally related to treatment / all	2 / 5	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 1	
Varicella zoster virus infection			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular device infection			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral infection			
subjects affected / exposed	1 / 371 (0.27%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Whipple's disease			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Wound infection staphylococcal			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Alcohol intolerance			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Decreased appetite			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dehydration			

subjects affected / exposed	5 / 371 (1.35%)	7 / 371 (1.89%)	
occurrences causally related to treatment / all	2 / 5	1 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic complication			
subjects affected / exposed	1 / 371 (0.27%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic ketoacidosis			
subjects affected / exposed	1 / 371 (0.27%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic metabolic decompensation			
subjects affected / exposed	1 / 371 (0.27%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Electrolyte imbalance			
subjects affected / exposed	2 / 371 (0.54%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Failure to thrive			
subjects affected / exposed	2 / 371 (0.54%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	1 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gout			
subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypercalcaemia			
subjects affected / exposed	5 / 371 (1.35%)	2 / 371 (0.54%)	
occurrences causally related to treatment / all	0 / 7	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperglycaemia			

subjects affected / exposed	2 / 371 (0.54%)	3 / 371 (0.81%)	
occurrences causally related to treatment / all	2 / 2	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypervolaemia			
subjects affected / exposed	1 / 371 (0.27%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoalbuminaemia			
subjects affected / exposed	1 / 371 (0.27%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypocalcaemia			
subjects affected / exposed	4 / 371 (1.08%)	4 / 371 (1.08%)	
occurrences causally related to treatment / all	0 / 5	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoglycaemia			
subjects affected / exposed	1 / 371 (0.27%)	5 / 371 (1.35%)	
occurrences causally related to treatment / all	0 / 4	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypokalaemia			
subjects affected / exposed	1 / 371 (0.27%)	4 / 371 (1.08%)	
occurrences causally related to treatment / all	0 / 1	1 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypomagnesaemia			
subjects affected / exposed	0 / 371 (0.00%)	4 / 371 (1.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyponatraemia			
subjects affected / exposed	1 / 371 (0.27%)	2 / 371 (0.54%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypophosphataemia			

subjects affected / exposed	0 / 371 (0.00%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malnutrition			
subjects affected / exposed	1 / 371 (0.27%)	0 / 371 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tumour lysis syndrome			
subjects affected / exposed	1 / 371 (0.27%)	1 / 371 (0.27%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Ld Cohort	E-Ld Cohort	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	365 / 371 (98.38%)	364 / 371 (98.11%)	
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	26 / 371 (7.01%)	20 / 371 (5.39%)	
occurrences (all)	30	20	
Flushing			
subjects affected / exposed	17 / 371 (4.58%)	19 / 371 (5.12%)	
occurrences (all)	18	22	
Hypertension			
subjects affected / exposed	44 / 371 (11.86%)	54 / 371 (14.56%)	
occurrences (all)	60	100	
Hypotension			
subjects affected / exposed	44 / 371 (11.86%)	63 / 371 (16.98%)	
occurrences (all)	51	86	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	73 / 371 (19.68%)	88 / 371 (23.72%)	
occurrences (all)	108	137	
Chest pain			

subjects affected / exposed	32 / 371 (8.63%)	24 / 371 (6.47%)	
occurrences (all)	39	30	
Chills			
subjects affected / exposed	9 / 371 (2.43%)	35 / 371 (9.43%)	
occurrences (all)	12	44	
Fatigue			
subjects affected / exposed	188 / 371 (50.67%)	183 / 371 (49.33%)	
occurrences (all)	279	288	
Influenza like illness			
subjects affected / exposed	28 / 371 (7.55%)	40 / 371 (10.78%)	
occurrences (all)	54	61	
Mucosal inflammation			
subjects affected / exposed	8 / 371 (2.16%)	21 / 371 (5.66%)	
occurrences (all)	8	28	
Non-cardiac chest pain			
subjects affected / exposed	19 / 371 (5.12%)	20 / 371 (5.39%)	
occurrences (all)	22	23	
Oedema			
subjects affected / exposed	19 / 371 (5.12%)	17 / 371 (4.58%)	
occurrences (all)	21	17	
Oedema peripheral			
subjects affected / exposed	182 / 371 (49.06%)	163 / 371 (43.94%)	
occurrences (all)	314	259	
Pain			
subjects affected / exposed	19 / 371 (5.12%)	24 / 371 (6.47%)	
occurrences (all)	36	27	
Peripheral swelling			
subjects affected / exposed	24 / 371 (6.47%)	24 / 371 (6.47%)	
occurrences (all)	30	25	
Pyrexia			
subjects affected / exposed	77 / 371 (20.75%)	111 / 371 (29.92%)	
occurrences (all)	167	211	
Respiratory, thoracic and mediastinal disorders			
Cough			

subjects affected / exposed	106 / 371 (28.57%)	120 / 371 (32.35%)	
occurrences (all)	168	191	
Dysphonia			
subjects affected / exposed	27 / 371 (7.28%)	45 / 371 (12.13%)	
occurrences (all)	30	49	
Dyspnoea			
subjects affected / exposed	93 / 371 (25.07%)	87 / 371 (23.45%)	
occurrences (all)	122	118	
Dyspnoea exertional			
subjects affected / exposed	18 / 371 (4.85%)	24 / 371 (6.47%)	
occurrences (all)	20	30	
Epistaxis			
subjects affected / exposed	18 / 371 (4.85%)	27 / 371 (7.28%)	
occurrences (all)	26	33	
Oropharyngeal pain			
subjects affected / exposed	26 / 371 (7.01%)	26 / 371 (7.01%)	
occurrences (all)	35	30	
Productive cough			
subjects affected / exposed	20 / 371 (5.39%)	33 / 371 (8.89%)	
occurrences (all)	24	43	
Psychiatric disorders			
Agitation			
subjects affected / exposed	17 / 371 (4.58%)	21 / 371 (5.66%)	
occurrences (all)	21	23	
Anxiety			
subjects affected / exposed	28 / 371 (7.55%)	44 / 371 (11.86%)	
occurrences (all)	33	50	
Confusional state			
subjects affected / exposed	32 / 371 (8.63%)	37 / 371 (9.97%)	
occurrences (all)	35	43	
Depression			
subjects affected / exposed	31 / 371 (8.36%)	42 / 371 (11.32%)	
occurrences (all)	35	45	
Insomnia			
subjects affected / exposed	96 / 371 (25.88%)	98 / 371 (26.42%)	
occurrences (all)	112	129	

Mood altered subjects affected / exposed occurrences (all)	17 / 371 (4.58%) 33	25 / 371 (6.74%) 26	
Investigations			
Alanine aminotransferase increased subjects affected / exposed occurrences (all)	27 / 371 (7.28%) 38	18 / 371 (4.85%) 24	
Aspartate aminotransferase increased subjects affected / exposed occurrences (all)	21 / 371 (5.66%) 27	17 / 371 (4.58%) 25	
Blood creatinine increased subjects affected / exposed occurrences (all)	72 / 371 (19.41%) 111	56 / 371 (15.09%) 85	
Neutrophil count decreased subjects affected / exposed occurrences (all)	28 / 371 (7.55%) 55	11 / 371 (2.96%) 27	
Glomerular filtration rate decreased subjects affected / exposed occurrences (all)	17 / 371 (4.58%) 35	20 / 371 (5.39%) 37	
Platelet count decreased subjects affected / exposed occurrences (all)	20 / 371 (5.39%) 58	12 / 371 (3.23%) 17	
Weight decreased subjects affected / exposed occurrences (all)	66 / 371 (17.79%) 78	79 / 371 (21.29%) 93	
Injury, poisoning and procedural complications			
Contusion subjects affected / exposed occurrences (all)	53 / 371 (14.29%) 72	47 / 371 (12.67%) 60	
Fall subjects affected / exposed occurrences (all)	32 / 371 (8.63%) 49	33 / 371 (8.89%) 46	
Skin abrasion subjects affected / exposed occurrences (all)	13 / 371 (3.50%) 15	24 / 371 (6.47%) 29	
Skin laceration			

subjects affected / exposed occurrences (all)	23 / 371 (6.20%) 31	19 / 371 (5.12%) 26	
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	25 / 371 (6.74%)	28 / 371 (7.55%)	
occurrences (all)	29	35	
Nervous system disorders			
Dizziness			
subjects affected / exposed	68 / 371 (18.33%)	84 / 371 (22.64%)	
occurrences (all)	102	124	
Dysgeusia			
subjects affected / exposed	13 / 371 (3.50%)	26 / 371 (7.01%)	
occurrences (all)	15	29	
Headache			
subjects affected / exposed	50 / 371 (13.48%)	61 / 371 (16.44%)	
occurrences (all)	73	85	
Hypoaesthesia			
subjects affected / exposed	25 / 371 (6.74%)	24 / 371 (6.47%)	
occurrences (all)	28	28	
Memory impairment			
subjects affected / exposed	15 / 371 (4.04%)	27 / 371 (7.28%)	
occurrences (all)	16	28	
Neuropathy peripheral			
subjects affected / exposed	48 / 371 (12.94%)	41 / 371 (11.05%)	
occurrences (all)	54	48	
Paraesthesia			
subjects affected / exposed	45 / 371 (12.13%)	40 / 371 (10.78%)	
occurrences (all)	55	65	
Peripheral sensory neuropathy			
subjects affected / exposed	59 / 371 (15.90%)	57 / 371 (15.36%)	
occurrences (all)	71	70	
Syncope			
subjects affected / exposed	20 / 371 (5.39%)	18 / 371 (4.85%)	
occurrences (all)	23	22	
Taste disorder			

subjects affected / exposed	27 / 371 (7.28%)	24 / 371 (6.47%)	
occurrences (all)	27	24	
Tremor			
subjects affected / exposed	55 / 371 (14.82%)	61 / 371 (16.44%)	
occurrences (all)	69	72	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	160 / 371 (43.13%)	153 / 371 (41.24%)	
occurrences (all)	325	338	
Leukopenia			
subjects affected / exposed	37 / 371 (9.97%)	23 / 371 (6.20%)	
occurrences (all)	141	83	
Neutropenia			
subjects affected / exposed	117 / 371 (31.54%)	93 / 371 (25.07%)	
occurrences (all)	397	286	
Thrombocytopenia			
subjects affected / exposed	69 / 371 (18.60%)	66 / 371 (17.79%)	
occurrences (all)	153	178	
Eye disorders			
Cataract			
subjects affected / exposed	56 / 371 (15.09%)	61 / 371 (16.44%)	
occurrences (all)	64	70	
Vision blurred			
subjects affected / exposed	28 / 371 (7.55%)	28 / 371 (7.55%)	
occurrences (all)	30	29	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	51 / 371 (13.75%)	50 / 371 (13.48%)	
occurrences (all)	66	76	
Abdominal pain upper			
subjects affected / exposed	29 / 371 (7.82%)	33 / 371 (8.89%)	
occurrences (all)	37	40	
Constipation			
subjects affected / exposed	144 / 371 (38.81%)	142 / 371 (38.27%)	
occurrences (all)	215	230	
Diarrhoea			

subjects affected / exposed	180 / 371 (48.52%)	192 / 371 (51.75%)	
occurrences (all)	399	476	
Dry mouth			
subjects affected / exposed	26 / 371 (7.01%)	28 / 371 (7.55%)	
occurrences (all)	31	30	
Dyspepsia			
subjects affected / exposed	32 / 371 (8.63%)	43 / 371 (11.59%)	
occurrences (all)	34	58	
Haemorrhoids			
subjects affected / exposed	19 / 371 (5.12%)	10 / 371 (2.70%)	
occurrences (all)	21	10	
Nausea			
subjects affected / exposed	108 / 371 (29.11%)	117 / 371 (31.54%)	
occurrences (all)	161	189	
Toothache			
subjects affected / exposed	15 / 371 (4.04%)	24 / 371 (6.47%)	
occurrences (all)	18	30	
Vomiting			
subjects affected / exposed	50 / 371 (13.48%)	69 / 371 (18.60%)	
occurrences (all)	72	119	
Skin and subcutaneous tissue disorders			
Dry skin			
subjects affected / exposed	22 / 371 (5.93%)	27 / 371 (7.28%)	
occurrences (all)	24	27	
Erythema			
subjects affected / exposed	21 / 371 (5.66%)	19 / 371 (5.12%)	
occurrences (all)	24	19	
Night sweats			
subjects affected / exposed	15 / 371 (4.04%)	24 / 371 (6.47%)	
occurrences (all)	21	29	
Hyperhidrosis			
subjects affected / exposed	26 / 371 (7.01%)	36 / 371 (9.70%)	
occurrences (all)	32	43	
Pruritus			
subjects affected / exposed	43 / 371 (11.59%)	39 / 371 (10.51%)	
occurrences (all)	50	48	

Rash			
subjects affected / exposed	86 / 371 (23.18%)	90 / 371 (24.26%)	
occurrences (all)	113	132	
Skin lesion			
subjects affected / exposed	17 / 371 (4.58%)	19 / 371 (5.12%)	
occurrences (all)	21	25	
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	19 / 371 (5.12%)	16 / 371 (4.31%)	
occurrences (all)	23	19	
Pollakiuria			
subjects affected / exposed	19 / 371 (5.12%)	14 / 371 (3.77%)	
occurrences (all)	20	14	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	121 / 371 (32.61%)	111 / 371 (29.92%)	
occurrences (all)	189	171	
Bone pain			
subjects affected / exposed	57 / 371 (15.36%)	58 / 371 (15.63%)	
occurrences (all)	75	75	
Back pain			
subjects affected / exposed	136 / 371 (36.66%)	133 / 371 (35.85%)	
occurrences (all)	209	214	
Joint swelling			
subjects affected / exposed	18 / 371 (4.85%)	19 / 371 (5.12%)	
occurrences (all)	21	19	
Muscle spasms			
subjects affected / exposed	83 / 371 (22.37%)	84 / 371 (22.64%)	
occurrences (all)	112	110	
Muscular weakness			
subjects affected / exposed	52 / 371 (14.02%)	45 / 371 (12.13%)	
occurrences (all)	58	56	
Musculoskeletal chest pain			
subjects affected / exposed	50 / 371 (13.48%)	49 / 371 (13.21%)	
occurrences (all)	60	66	
Musculoskeletal pain			

subjects affected / exposed	21 / 371 (5.66%)	28 / 371 (7.55%)	
occurrences (all)	24	29	
Myalgia			
subjects affected / exposed	17 / 371 (4.58%)	22 / 371 (5.93%)	
occurrences (all)	18	27	
Neck pain			
subjects affected / exposed	37 / 371 (9.97%)	30 / 371 (8.09%)	
occurrences (all)	43	37	
Pain in jaw			
subjects affected / exposed	12 / 371 (3.23%)	19 / 371 (5.12%)	
occurrences (all)	12	23	
Pain in extremity			
subjects affected / exposed	78 / 371 (21.02%)	76 / 371 (20.49%)	
occurrences (all)	97	118	
Spinal pain			
subjects affected / exposed	23 / 371 (6.20%)	15 / 371 (4.04%)	
occurrences (all)	31	19	
Infections and infestations			
Cystitis			
subjects affected / exposed	20 / 371 (5.39%)	13 / 371 (3.50%)	
occurrences (all)	22	14	
Cellulitis			
subjects affected / exposed	26 / 371 (7.01%)	21 / 371 (5.66%)	
occurrences (all)	30	26	
Bronchitis			
subjects affected / exposed	52 / 371 (14.02%)	46 / 371 (12.40%)	
occurrences (all)	95	99	
Influenza			
subjects affected / exposed	20 / 371 (5.39%)	14 / 371 (3.77%)	
occurrences (all)	31	18	
Herpes zoster			
subjects affected / exposed	18 / 371 (4.85%)	23 / 371 (6.20%)	
occurrences (all)	19	23	
Nasopharyngitis			
subjects affected / exposed	62 / 371 (16.71%)	60 / 371 (16.17%)	
occurrences (all)	129	120	

Oral herpes			
subjects affected / exposed	11 / 371 (2.96%)	23 / 371 (6.20%)	
occurrences (all)	20	29	
Pneumonia			
subjects affected / exposed	23 / 371 (6.20%)	33 / 371 (8.89%)	
occurrences (all)	29	37	
Sinusitis			
subjects affected / exposed	17 / 371 (4.58%)	23 / 371 (6.20%)	
occurrences (all)	20	32	
Respiratory tract infection			
subjects affected / exposed	34 / 371 (9.16%)	38 / 371 (10.24%)	
occurrences (all)	67	90	
Upper respiratory tract infection			
subjects affected / exposed	84 / 371 (22.64%)	82 / 371 (22.10%)	
occurrences (all)	162	142	
Urinary tract infection			
subjects affected / exposed	56 / 371 (15.09%)	58 / 371 (15.63%)	
occurrences (all)	111	114	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	86 / 371 (23.18%)	100 / 371 (26.95%)	
occurrences (all)	113	117	
Dehydration			
subjects affected / exposed	22 / 371 (5.93%)	25 / 371 (6.74%)	
occurrences (all)	24	29	
Hyperglycaemia			
subjects affected / exposed	69 / 371 (18.60%)	120 / 371 (32.35%)	
occurrences (all)	121	255	
Hypoalbuminaemia			
subjects affected / exposed	21 / 371 (5.66%)	24 / 371 (6.47%)	
occurrences (all)	36	61	
Hypokalaemia			
subjects affected / exposed	91 / 371 (24.53%)	84 / 371 (22.64%)	
occurrences (all)	183	175	
Hypocalcaemia			

subjects affected / exposed	75 / 371 (20.22%)	73 / 371 (19.68%)	
occurrences (all)	169	160	
Hypomagnesaemia			
subjects affected / exposed	23 / 371 (6.20%)	41 / 371 (11.05%)	
occurrences (all)	32	67	
Hypophosphataemia			
subjects affected / exposed	16 / 371 (4.31%)	20 / 371 (5.39%)	
occurrences (all)	25	36	
Hyponatraemia			
subjects affected / exposed	17 / 371 (4.58%)	27 / 371 (7.28%)	
occurrences (all)	20	37	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
15 March 2012	<p>Clarification of subject eligibility or study procedures.</p> <p>Modification of screening requirements to conform to the standard of care and to enhance overall study conduct.</p> <p>A revision was made to timing of when pregnancy testing must be completed. This change is in compliance with a recently approved, company-wide SOP for women of childbearing potential participating in clinical trials conducted by the Sponsor.</p> <p>The inclusion criteria have been revised to clarify that refusal to undergo high dose therapy with SCT is NOT sufficient for entry onto 006 for a subject < 65 years old. There must be a comorbidity that prevents SCT for a subject < 65 years old.</p> <p>Instructions for what should be done with missed doses of lenalidomide or dexamethasone.</p> <p>Revisions are made to exclusion criteria for clarity and consistency throughout the development program.</p> <p>The requirement to discontinue elotuzumab and lenalidomide if a subject becomes pregnant.</p> <p>Timing and details surrounding when certain study assessments are performed.</p> <p>An update to the shelf-life of reconstituted elotuzumab.</p> <p>Correction of typographical errors.</p>
21 May 2014	<p>Elotuzumab infusion rate escalation plan added to decrease the infusion of elotuzumab to approximately 1 hour</p> <p>Change to the UPEP efficacy testing to reduce the requirement of 24 hour urine collection in a subset of patients</p> <p>Broadening of the medications that can be used for thromboprophylaxis.</p> <p>Additional Clarifications in the protocol serve to reduce any ambiguity regarding study procedures, and provide additional guidance of the EBMT efficacy requirements.</p>
21 August 2014	<p>Planned Interim Analysis will now take place at 70% of events (338 events) compared to the previous timepoint of 241 (50%) progression events</p> <p>BPI-SF pain severity and pain interference will be evaluated as a secondary endpoint, and formal comparison between treatment arms will be conducted, though it will not be included hierarchical testing.</p> <p>Addition of exploratory objectives to assess PFS at 1, 2 and 3 years and OS rates at 3, 4, 5 and 6 years.</p> <p>Correction of typographical errors in the protocol and appendix documents.</p>
17 August 2015	<p>Update statistical assumptions and protocol treatment rationale based on currently available published data</p> <p>Clarify requirements for subjects with no measureable urine M protein at baseline</p> <p>Inclusion of new PK/HAHA collection after Cycle 18</p> <p>Inclusion of updated safety information regarding use of adequate contraception based on recent elotuzumab PK data.</p> <p>Change recommended diluent volume of elotuzumab from fixed volumes to range of 100-500 mL.</p>

24 August 2016	<p>To promote PFS rates from an exploratory objective to a secondary objective, and to expand the assessment of PFS rates from 1,2,3 years to cover years 1-5, inclusive.</p> <p>Add Time-to-next-treatment (TTNT) as exploratory objective</p> <p>Remove the following sentence from Section 4.3.1. "On the days of elotuzumab administration, the dose of lenalidomide is to be administered at least 2 hours after completion of elotuzumab dosing.</p> <p>Change referencing of Experimental treatment arm of lenalidomide/dexamethasone + elotuzumab from LdE to E-Ld.</p> <p>Add Section 8.3.7-Time to Next Treatment (TTNT)</p> <p>Add Section 9.1.2.1 Source Documentation</p> <p>Update Section 9.2.2 Study Drug Records</p>
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Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported