



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
Arm title	E-Ld cohort

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
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Dictionary version	MedDRA24.1
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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	
Sebaceous 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	
Hydrocholecystitis			
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 occurrences (all)	106 / 371 (28.57%) 168	120 / 371 (32.35%) 191	
Dysphonia subjects affected / exposed occurrences (all)	27 / 371 (7.28%) 30	45 / 371 (12.13%) 49	
Dyspnoea subjects affected / exposed occurrences (all)	93 / 371 (25.07%) 122	87 / 371 (23.45%) 118	
Dyspnoea exertional subjects affected / exposed occurrences (all)	18 / 371 (4.85%) 20	24 / 371 (6.47%) 30	
Epistaxis subjects affected / exposed occurrences (all)	18 / 371 (4.85%) 26	27 / 371 (7.28%) 33	
Oropharyngeal pain subjects affected / exposed occurrences (all)	26 / 371 (7.01%) 35	26 / 371 (7.01%) 30	
Productive cough subjects affected / exposed occurrences (all)	20 / 371 (5.39%) 24	33 / 371 (8.89%) 43	
Psychiatric disorders			
Agitation subjects affected / exposed occurrences (all)	17 / 371 (4.58%) 21	21 / 371 (5.66%) 23	
Anxiety subjects affected / exposed occurrences (all)	28 / 371 (7.55%) 33	44 / 371 (11.86%) 50	
Confusional state subjects affected / exposed occurrences (all)	32 / 371 (8.63%) 35	37 / 371 (9.97%) 43	
Depression subjects affected / exposed occurrences (all)	31 / 371 (8.36%) 35	42 / 371 (11.32%) 45	
Insomnia subjects affected / exposed occurrences (all)	96 / 371 (25.88%) 112	98 / 371 (26.42%) 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 occurrences (all)	27 / 371 (7.28%) 27	24 / 371 (6.47%) 24	
Tremor subjects affected / exposed occurrences (all)	55 / 371 (14.82%) 69	61 / 371 (16.44%) 72	
Blood and lymphatic system disorders			
Anaemia subjects affected / exposed occurrences (all)	160 / 371 (43.13%) 325	153 / 371 (41.24%) 338	
Leukopenia subjects affected / exposed occurrences (all)	37 / 371 (9.97%) 141	23 / 371 (6.20%) 83	
Neutropenia subjects affected / exposed occurrences (all)	117 / 371 (31.54%) 397	93 / 371 (25.07%) 286	
Thrombocytopenia subjects affected / exposed occurrences (all)	69 / 371 (18.60%) 153	66 / 371 (17.79%) 178	
Eye disorders			
Cataract subjects affected / exposed occurrences (all)	56 / 371 (15.09%) 64	61 / 371 (16.44%) 70	
Vision blurred subjects affected / exposed occurrences (all)	28 / 371 (7.55%) 30	28 / 371 (7.55%) 29	
Gastrointestinal disorders			
Abdominal pain subjects affected / exposed occurrences (all)	51 / 371 (13.75%) 66	50 / 371 (13.48%) 76	
Abdominal pain upper subjects affected / exposed occurrences (all)	29 / 371 (7.82%) 37	33 / 371 (8.89%) 40	
Constipation subjects affected / exposed occurrences (all)	144 / 371 (38.81%) 215	142 / 371 (38.27%) 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 occurrences (all)	21 / 371 (5.66%) 24	28 / 371 (7.55%) 29	
Myalgia			
subjects affected / exposed occurrences (all)	17 / 371 (4.58%) 18	22 / 371 (5.93%) 27	
Neck pain			
subjects affected / exposed occurrences (all)	37 / 371 (9.97%) 43	30 / 371 (8.09%) 37	
Pain in jaw			
subjects affected / exposed occurrences (all)	12 / 371 (3.23%) 12	19 / 371 (5.12%) 23	
Pain in extremity			
subjects affected / exposed occurrences (all)	78 / 371 (21.02%) 97	76 / 371 (20.49%) 118	
Spinal pain			
subjects affected / exposed occurrences (all)	23 / 371 (6.20%) 31	15 / 371 (4.04%) 19	
Infections and infestations			
Cystitis			
subjects affected / exposed occurrences (all)	20 / 371 (5.39%) 22	13 / 371 (3.50%) 14	
Cellulitis			
subjects affected / exposed occurrences (all)	26 / 371 (7.01%) 30	21 / 371 (5.66%) 26	
Bronchitis			
subjects affected / exposed occurrences (all)	52 / 371 (14.02%) 95	46 / 371 (12.40%) 99	
Influenza			
subjects affected / exposed occurrences (all)	20 / 371 (5.39%) 31	14 / 371 (3.77%) 18	
Herpes zoster			
subjects affected / exposed occurrences (all)	18 / 371 (4.85%) 19	23 / 371 (6.20%) 23	
Nasopharyngitis			
subjects affected / exposed occurrences (all)	62 / 371 (16.71%) 129	60 / 371 (16.17%) 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	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. Add Time-to-next-treatment (TTNT) as exploratory objective 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." Change referencing of Experimental treatment arm of lenalidomide/dexamethasone + elotuzumab from LdE to E-Ld. Add Section 8.3.7-Time to Next Treatment (TTNT) Add Section 9.1.2.1 Source Documentation Update Section 9.2.2 Study Drug Records
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Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported