Clinical trial results:
A Phase 3 Randomized, Double-blind, Placebo-controlled, Multicenter Study of AMG 386 With Paclitaxel and Carboplatin as First-line Treatment of Subjects With FIGO Stage III-IV Epithelial Ovarian, Primary Peritoneal or Fallopian Tube Cancers

Summary

EudraCT number	2011-001112-53
Trial protocol	GR ES BE NL AT DK IT DE
Global end of trial date	05 December 2016

Results information

Result version number	v1 (current)
This version publication date	20 December 2017
First version publication date	20 December 2017

Trial information

Trial identification

Sponsor protocol code	20101129

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01493505
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Amgen Inc.
Sponsor organisation address	One Amgen Center Drive, Thousand Oaks, CA, United States, 91320
Public contact	IHQ Medical Info-Clinical Trials, Amgen (EUROPE) GmbH, MedInfoInternational@amgen.com
Scientific contact	IHQ Medical Info-Clinical Trials, Amgen (EUROPE) GmbH, MedInfoInternational@amgen.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	05 December 2016
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	05 December 2016
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study was to determine if 6 cycles of paclitaxel and carboplatin plus trebananib followed by 18 months of trebananib maintenance improves progression-free survival compared with 6 cycles of paclitaxel and carboplatin plus placebo followed by 18 months of placebo maintenance in the first-line treatment of patients with International Federation of Gynecology and Obstetrics (FIGO) stage III-IV epithelial ovarian, primary peritoneal, or fallopian tube cancers.

Protection of trial subjects:

This study was conducted in accordance with International Conference on Harmonisation (ICH) Good Clinical Practice (GCP) regulations/guidelines. Essential documents will be retained in accordance with ICH GCP.
All subjects provided written informed consent before undergoing any study-related procedures, including screening procedures.
The study protocol, amendments, and the informed consent form (ICF) were reviewed by the Institutional Review Boards (IRBs) and Independent Ethics Committees (IECs). No subjects were recruited into the study and no investigational product (IP) was shipped until the IRB/IEC gave written approval of the protocol and ICF and Amgen received copies of these approvals.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	30 January 2012
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	75 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Canada: 25
Country: Number of subjects enrolled	United States: 299
Country: Number of subjects enrolled	Austria: 22
Country: Number of subjects enrolled	Belgium: 89
Country: Number of subjects enrolled	Denmark: 20
Country: Number of subjects enrolled	Germany: 62
Country: Number of subjects enrolled	Greece: 49
Country: Number of subjects enrolled	Italy: 102
Country: Number of subjects enrolled	Netherlands: 8
Country: Number of subjects enrolled	Spain: 97
Country: Number of subjects enrolled	Hong Kong: 23
Country: Number of subjects enrolled	Japan: 51

Country: Number of subjects enrolled	Korea, Republic of: 75
Country: Number of subjects enrolled	Russian Federation: 93
Worldwide total number of subjects	1015
EEA total number of subjects	449

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)	702
From 65 to 84 years	312
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

This study was conducted at 206 centers in Asia, Australia, Canada, Russia, the United States, and Western Europe. Participants were enrolled from 30 January 2012 until 25 February 2014.

Pre-assignment

Screening details:

Participants were randomized in a 2:1 ratio to receive either trebananib, paclitaxel and carboplatin or placebo, paclitaxel and carboplatin. Randomization was stratified based on carboplatin dose and FIGO disease stage and either category of residual disease after primary debulking surgery (PDS) or planned interval debulking surgery (IDS).

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Investigator, Subject

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo + Paclitaxel + Carboplatin

Arm description:

Participants received placebo intravenous (IV) infusion once a week, paclitaxel 175 mg/m² by IV infusion once every 3 weeks (Q3W), and carboplatin at an area under the curve (AUC) 5 or 6 IV Q3W for 6 cycles followed by placebo IV once a week maintenance for 18 months.

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

Dosage and administration details:

Administered intravenously once every week

Investigational medicinal product name	Paclitaxel
Investigational medicinal product code	
Other name	Taxol®
Pharmaceutical forms	Concentrate for solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Paclitaxel 175 mg/m², administered as an intravenous infusion over 3 hours.

Investigational medicinal product name	Carboplatin
Investigational medicinal product code	
Other name	Paraplatin®
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Carboplatin was dosed using the glomerular filtration rate (GFR) and Calvert formula to an AUC/time curve of 5 or 6 administered by intravenous infusion.

Arm title	Trebananib + Paclitaxel + Carboplatin

Arm description:

Participants received trebananib 15 mg/kg IV once a week, paclitaxel 175 mg/m² infusion Q3W, and

carboplatin AUC 5 or 6 IV Q3W for 6 cycles followed by trebananib 15 mg/kg IV once a week maintenance for 18 months.

Arm type	Experimental
Investigational medicinal product name	Trebananib
Investigational medicinal product code	AMG 386
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Trebananib 15 mg/kg administered intravenously once every week

Investigational medicinal product name	Carboplatin
Investigational medicinal product code	
Other name	Paraplatin®
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Carboplatin was dosed using the glomerular filtration rate (GFR) and Calvert formula to an AUC/time curve of 5 or 6 administered by intravenous infusion.

Investigational medicinal product name	Paclitaxel
Investigational medicinal product code	
Other name	Taxol®
Pharmaceutical forms	Concentrate for solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Paclitaxel 175 mg/m², administered as an intravenous infusion over 3 hours.

Number of subjects in period 1	Placebo + Paclitaxel + Carboplatin	Trebananib + Paclitaxel + Carboplatin
Started	337	678
Received trebananib/placebo	332	663
Received paclitaxel	336	670
Received carboplatin	337	671
Completed	0	0
Not completed	337	678
Consent withdrawn by subject	29	79
Death	134	262
Other	166	319
Lost to follow-up	8	18

Baseline characteristics

Reporting groups	
Reporting group title	Placebo + Paclitaxel + Carboplatin
Reporting group description:	
Participants received placebo intravenous (IV) infusion once a week, paclitaxel 175 mg/m² by IV infusion once every 3 weeks (Q3W), and carboplatin at an area under the curve (AUC) 5 or 6 IV Q3W for 6 cycles followed by placebo IV once a week maintenance for 18 months.	
Reporting group title	Trebananib + Paclitaxel + Carboplatin
Reporting group description:	
Participants received trebananib 15 mg/kg IV once a week, paclitaxel 175 mg/m² infusion Q3W, and carboplatin AUC 5 or 6 IV Q3W for 6 cycles followed by trebananib 15 mg/kg IV once a week maintenance for 18 months.	

Reporting group values	Placebo + Paclitaxel + Carboplatin	Trebananib + Paclitaxel + Carboplatin	Total
Number of subjects	337	678	1015
Age Categorical Units: Subjects			
Adults (18-64 years)	231	471	702
From 65-84 years	105	207	312
85 years and over	1	0	1
Age Continuous Units: years			
arithmetic mean	58.4	58.4	
standard deviation	± 10.9	± 10.8	-
Gender Categorical Units: Subjects			
Female	337	678	1015
Male	0	0	0
Cancer Type Units: Subjects			
Ovarian cancer	290	583	873
Primary peritoneal carcinoma	31	65	96
Fallopian tube cancer	16	29	45
Not available	0	1	1
Stratification Factor: Carboplatin Dose Units: Subjects			
AUC 5	156	317	473
AUC 6	181	361	542
Stratification Factor: FIGO Stage Units: Subjects			
Stage IIIA/IIIB	30	60	90
Stage IIIC/IV	307	618	925
Stratification Factor: Debulking Surgery Units: Subjects			
Received PDS: Optimally debulked	118	238	356
Received PDS: Suboptimally debulked	95	193	288
Planning for IDS	124	247	371

End points

End points reporting groups

Reporting group title	Placebo + Paclitaxel + Carboplatin
Reporting group description:	
Participants received placebo intravenous (IV) infusion once a week, paclitaxel 175 mg/m² by IV infusion once every 3 weeks (Q3W), and carboplatin at an area under the curve (AUC) 5 or 6 IV Q3W for 6 cycles followed by placebo IV once a week maintenance for 18 months.	
Reporting group title	Trebananib + Paclitaxel + Carboplatin
Reporting group description:	
Participants received trebananib 15 mg/kg IV once a week, paclitaxel 175 mg/m² infusion Q3W, and carboplatin AUC 5 or 6 IV Q3W for 6 cycles followed by trebananib 15 mg/kg IV once a week maintenance for 18 months.	

Primary: Progression-free Survival

End point title	Progression-free Survival
End point description:	
Progression-free survival (PFS) was defined as the time from randomization to the earliest of disease progression per Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1 with modifications or death from any cause. Subjects not meeting these criteria by the analysis data cutoff date were censored at their last radiographic-evaluable disease assessment date. Events of radiographic progression that occurred after the initiation of subsequent anticancer therapy were not considered PFS events and were censored at the last radiographic assessment before the initiation of subsequent anticancer therapy. Deaths occurring after initiation of subsequent anticancer therapy were considered PFS events. Tumor response was determined by the investigator. Progressive disease was defined as at least a 20% increase in the size of target lesions, with an absolute increase of at least 5 mm, or unequivocal progression of existing non-target lesions.	
End point type	Primary
End point timeframe:	
From randomization to the data cut-off date; median overall study follow-up time was 151.3 weeks in both treatment groups.	

End point values	Placebo + Paclitaxel + Carboplatin	Trebananib + Paclitaxel + Carboplatin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	337	678		
Units: months				
median (confidence interval 95%)	15.1 (12.7 to 16.4)	16.7 (15.0 to 17.7)		

Statistical analyses

Statistical analysis title	Analysis of Progression-free Survival
Comparison groups	Placebo + Paclitaxel + Carboplatin v Trebananib + Paclitaxel + Carboplatin

Number of subjects included in analysis	1015
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.31 [1]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.92
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.78
upper limit	1.08

Notes:

[1] - Log-rank test stratified by the stratification factors FIGO disease stage and category of residual disease after PDS or planned IDS

Secondary: Overall Survival

End point title	Overall Survival

End point description:

Overall survival was defined as the time from the randomization date to the date of death from any cause. Subjects who were lost to follow-up before the analysis data cutoff date or were alive by the analysis data cutoff date were censored at their last contact date (last known to be alive).
"99999" indicates values that could not be estimated.

End point type	Secondary

End point timeframe:

From randomization to the data cut-off date; median overall study follow-up time was 151.3 weeks in both treatment groups.

End point values	Placebo + Paclitaxel + Carboplatin	Trebananib + Paclitaxel + Carboplatin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	337	678		
Units: months				
median (confidence interval 95%)	48.8 (43.1 to 99999)	48.8 (44.7 to 99999)		

Statistical analyses

Statistical analysis title	Overall Survival Analysis
Comparison groups	Placebo + Paclitaxel + Carboplatin v Trebananib + Paclitaxel + Carboplatin
Number of subjects included in analysis	1015
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.87 [2]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.02

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.83
upper limit	1.25

Notes:

[2] - Log rank test stratified by FIGO disease stage and category of residual disease after PDS or planned IDS.

Secondary: Number of Participants with Adverse Events

End point title	Number of Participants with Adverse Events

End point description:

Adverse events were graded for severity according to the Common Terminology Criteria for Adverse Events (CTCAE) version 3.0 grading scale, except edema AE. The investigator assessed whether each adverse event was possibly related to the trebananib / placebo and/or paclitaxel or carboplatin.

The safety analysis set was defined as the subset of randomized subjects who received at least 1 dose of any study drug. One subject randomized to the placebo group received trebananib and was included in the trebananib group for safety analysis.

End point type	Secondary

End point timeframe:

From first dose of any study treatment until 30 days after the last dose; median duration was 338 days for the placebo group and 251 days for trebananib group.

End point values	Placebo + Paclitaxel + Carboplatin	Trebananib + Paclitaxel + Carboplatin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	336	675		
Units: participants				
Any adverse event (AE)	327	666		
Grade ≥ 3	237	510		
Grade ≥ 4	102	227		
Fatal adverse events	1	20		
Serious adverse events (SAE)	104	269		
AE leading to discontinuation of trebananib	44	186		
SAE leading to discontinuation of trebananib	15	60		
AE leading to discontinuation of paclitaxel	29	63		
SAE leading to discontinuation of paclitaxel	10	17		
AE leading to discontinuation of carboplatin	28	49		
SAE leading to discontinuation of carboplatin	8	16		
AE leading to discontinuation from all study drugs	16	30		
SAE leading to discontinuation of all study drugs	7	14		
Trebananib-related adverse events	207	516		
Paclitaxel-related adverse events	316	649		
Carboplatin-related adverse events	310	632		

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Observed Concentration (Cmax) of Trebananib

End point title	Maximum Observed Concentration (Cmax) of Trebananib[3]

End point description:

Trebananib pharmacokinetic (PK) concentrations below the lower limit of quantification of 20 ng/mL were set to 0 before data analysis. Week 7 values were based on subjects with 3 consecutive doses to ensure the steady state was reached.
The PK analysis set was defined as a subset of subjects in the safety analysis set who had evaluable concentration data.

End point type	Secondary

End point timeframe:

Week 1 (after single administration) and week 7 (at steady state), at the end of infusion

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: PK analyses were only performed in subjects in the trebananib treatment group.

End point values	Trebananib + Paclitaxel + Carboplatin			
Subject group type	Reporting group			
Number of subjects analysed	537[4]			
Units: µg/mL				
arithmetic mean (standard deviation)				
Week 1 (n = 537)	271 (± 114)			
Week 7 (n = 441)	309 (± 119)			

Notes:

[4] - PK analysis set with available data at each time point

Statistical analyses

No statistical analyses for this end point

Secondary: Minimum Observed Concentration (Cmin) of Trebananib

End point title	Minimum Observed Concentration (Cmin) of Trebananib[5]

End point description:

Week 7 values were based on subjects with 3 consecutive doses to ensure the steady state was reached. Such criterion was not implemented for weeks 10 and 19.
Week 10 Cmin values include only primary debulking surgery subjects

End point type	Secondary

End point timeframe:

Weeks 7, 10, and 19, predose

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: PK analyses were only performed in subjects in the trebananib treatment group.

End point values	Trebananib + Paclitaxel + Carboplatin			
Subject group type	Reporting group			
Number of subjects analysed	438[6]			
Units: µg/mL				
arithmetic mean (standard deviation)				
Week 7 (n = 438)	24.3 (± 14.4)			
Week 10 (n = 297)	24.1 (± 17.6)			
Week 19 (n = 386)	25.6 (± 16.6)			

Notes:

[6] - PK analysis set with available data at each time point

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants who Developed Anti-Trebananib Antibodies

End point title	Number of Participants who Developed Anti-Trebananib Antibodies

End point description:

Participants who developed antibody binding are defined as participants with a negative result at baseline and a positive result post-baseline.

End point type	Secondary

End point timeframe:

Day 1 of weeks 1, 10, 19, and 30 days after last dose

End point values	Placebo + Paclitaxel + Carboplatin	Trebananib + Paclitaxel + Carboplatin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	309[7]	594[8]		
Units: participants				
Binding antibody positive	11	72		
Neutralizing antibody positive	0	0		

Notes:

[7] - Subjects with a post-baseline result

[8] - Subjects with a post-baseline result

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Functional Assessment of Cancer Therapy – Ovary (FACT-O) Summary Score

End point title	Change from Baseline in Functional Assessment of Cancer

	Therapy – Ovary (FACT-O) Summary Score

End point description:

The FACT-O evaluates the health-related quality of life (HRQOL) and symptoms in patients with ovarian cancer. It consists of the FACT-G, a 27 item general cancer questionnaire and a 12-item ovarian cancer-specific subscale (OCS). Each item is scored by the participant on a scale from 0 (not at all true) to 4 (very much true). The total score ranges from 0 to 156; a higher total score indicates better quality of life or less severe symptoms.
The patient-reported outcomes (PRO) analysis set is defined as a subset of randomized subjects who have a baseline PRO assessment and at least one post-baseline PRO assessment prior to disease progression and the initiation of subsequent anticancer therapy.

End point type	Secondary

End point timeframe:

Baseline and Weeks 7, 13 and during the maintenance phase at months 3, 6, 9, 12, 15 and 18, and the safety follow-up visit 30 days after last dose.

End point values	Placebo + Paclitaxel + Carboplatin	Trebananib + Paclitaxel + Carboplatin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	293[9]	564[10]		
Units: units on a scale				
arithmetic mean (standard deviation)				
Week 7 (n = 272, 528)	4.4 (± 15.7)	0.7 (± 15.2)		
Week 13 (n = 250, 459)	5.5 (± 16.5)	0.7 (± 16.4)		
Month 3 (n = 190, 294)	12.1 (± 16.5)	8.9 (± 17.8)		
Month 6 (n = 142, 208)	13.7 (± 15.7)	9.2 (± 17.4)		
Month 9 (n = 98, 160)	13.1 (± 17.0)	8.4 (± 16.8)		
Month 12 (n = 70, 117)	14.0 (± 14.7)	8.2 (± 17.9)		
Month 15 (n = 45, 84)	10.1 (± 15.3)	9.3 (± 18.2)		
Month 18 (n = 7, 20)	19.4 (± 19.9)	14.1 (± 18.9)		
Safety follow-up (n = 69, 183)	13.1 (± 20.0)	4.5 (± 18.7)		

Notes:

[9] - PRO analysis set with available data at each time point

[10] - PRO analysis set with available data at each time point

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in FACT-O Ovarian Cancer-specific (OCS) Subscale

End point title	Change from Baseline in FACT-O Ovarian Cancer-specific (OCS) Subscale

End point description:

The FACT-O evaluates the health-related quality of life (HRQOL) and symptoms in patients with ovarian cancer. It consists of the FACT-G, a 27 item general cancer questionnaire and a 12-item ovarian cancer-specific subscale (OCS). The OCS consists of 12 symptom items including swelling in stomach area, cramps in stomach area, weight loss, hair loss, control of bowels, appetite, vomiting, ability to get around, liking the appearance of one’s body, being able to feel like a woman, interest in sex, and concern about ability to have children. Each item is scored by the participant on a scale from 0 (not at all true) to 4 (very much true). The OCS summary score ranges from 0 to 48, where a higher score indicates better quality of life or less severe symptoms.
The PRO analysis set includes a subset of randomized subjects who had a baseline PRO assessment and at least one post-baseline PRO assessment prior to disease progression and the initiation of subsequent anticancer therapy.

End point type	Secondary

End point timeframe:

Baseline and Weeks 7, 13 and during the maintenance phase at months 3, 6, 9, 12, 15 and 18, and the safety follow-up visit 30 days after last dose.

End point values	Placebo + Paclitaxel + Carboplatin	Trebananib + Paclitaxel + Carboplatin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	299[11]	581[12]		
Units: units on a scale				
arithmetic mean (standard deviation)				
Week 7 (n = 282, 554)	1.6 (± 5.1)	0.7 (± 5.3)		
Week 13 (n = 256, 477)	2.0 (± 5.7)	1.0 (± 5.6)		
Month 3 (n = 199, 305)	4.2 (± 6.0)	3.7 (± 6.1)		
Month 6 (n = 148, 219)	4.3 (± 5.8)	3.6 (± 6.1)		
Month 9 (n = 101, 165)	3.9 (± 6.1)	3.4 (± 5.7)		
Month 12 (n = 71, 120)	4.4 (± 4.6)	3.5 (± 6.3)		
Month 15 (n = 46, 85)	3.1 (± 5.7)	3.7 (± 6.2)		
Month 18 (n = 7, 21)	6.2 (± 7.2)	5.6 (± 6.7)		
Safety follow-up (n = 78, 195)	4.2 (± 7.3)	2.3 (± 6.3)		

Notes:

[11] - PRO analysis set with available data at each time point

[12] - PRO analysis set with available data at each time point

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in EuroQOL 5-Dimension (EQ-5D) Health Index Score

End point title	Change from Baseline in EuroQOL 5-Dimension (EQ-5D) Health Index Score

End point description:

The EQ-5D is a standardized instrument for use as a generic, preference-based measure of health outcome. The EQ-5D questionnaire captures two basic types of information, a descriptive “profile,” or “health state,” and an overall health rating using a visual analogue scale.
The health state includes five dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Each question has 3 answer choices: 1 (no problems), 2 (moderate problems), and 3 (extreme problems). The health states for each respondent are converted into a single index number using a specified set of weights. Resulting scores can range from 1.0 and –0.594. A higher score indicates a more preferred health status with 1.0 representing perfect health.
The PRO analysis set includes a subset of randomized subjects who had a baseline assessment and at least 1 post-baseline PRO assessment prior to disease progression and the initiation of subsequent anticancer therapy.

End point type	Secondary

End point timeframe:

Baseline and weeks 7 and 13, and maintenance phase months 3, 6, 9, 12, 15, and 18 and the safety follow-up visit 30 days after last dose.

End point values	Placebo + Paclitaxel + Carboplatin	Trebananib + Paclitaxel + Carboplatin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	290[13]	568[14]		
Units: units on a scale				
arithmetic mean (standard deviation)				
Week 7 (n = 269, 531)	0.1 (± 0.2)	0.0 (± 0.2)		
Week 13 (n = 245, 461)	0.1 (± 0.2)	0.0 (± 0.3)		
Month 3 (n = 192, 295)	0.1 (± 0.2)	0.1 (± 0.2)		
Month 6 (n = 140, 209)	0.8 (± 0.2)	0.8 (± 0.2)		
Month 9 (n = 96, 160)	0.1 (± 0.2)	0.1 (± 0.2)		
Month 12 (n = 68, 114)	0.1 (± 0.2)	0.1 (± 0.3)		
Month 15 (n = 44, 80)	0.1 (± 0.2)	0.1 (± 0.3)		
Month 18 (n = 7, 21)	0.4 (± 0.3)	0.2 (± 0.2)		
Safety follow-up (n = 76, 186)	0.1 (± 0.3)	0.0 (± 0.3)		

Notes:

[13] - PRO analysis set with available data at each time point

[14] - PRO analysis set with available data at each time point

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in EQ-5D Visual Analogue Scale Score

End point title	Change from Baseline in EQ-5D Visual Analogue Scale Score

End point description:

The EQ-5D is a standardized instrument for use as a generic, preference-based measure of health outcome. The EQ-5D questionnaire captures two basic types of information, a descriptive “profile,” or “health state,” and an overall health rating using a visual analogue scale (VAS).
The visual analogue scale asks respondents to rate their present health status on a 0 - 100 visual analogue scale, with 0 labeled as “Worst imaginable health state” and 100 labeled as “Best imaginable health state.” The VAS score is determined by observing the point at which the subjects hand drawn line intersects the scale.
The PRO analysis set includes the subset of randomized subjects who had a baseline assessment and at least 1 post-baseline PRO assessment prior to disease progression and the initiation of subsequent anticancer therapy.

End point type	Secondary

End point timeframe:

Baseline and weeks 7 and 13, and maintenance phase months 3, 6, 9, 12, 15, and 18 and the safety follow-up visit 30 days after last dose.

End point values	Placebo + Paclitaxel + Carboplatin	Trebananib + Paclitaxel + Carboplatin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	286[15]	563[16]		
Units: units on a scale				
arithmetic mean (standard deviation)				
Week 7 (n = 267, 523)	6.2 (± 18.4)	2.3 (± 18.5)		
Week 13 (n = 242, 457)	7.2 (± 18.0)	3.6 (± 18.3)		
Month 3 (n = 185, 289)	10.0 (± 20.3)	9.6 (± 19.1)		
Month 6 (n = 138, 211)	13.6 (± 17.1)	10.0 (± 20.3)		

Month 9 (n = 98,159)	12.7 (± 19.7)	10.4 (± 19.5)		
Month 12 (n = 66, 117)	14.1 (± 18.8)	11.1 (± 19.3)		
Month 15 (n = 43, 81)	12.7 (± 17.7)	11.6 (± 20.0)		
Month 12 (n = 6, 20)	20.8 (± 11.1)	22.5 (± 24.1)		
Safety follow-up (n = 78, 188)	14.1 (± 20.9)	6.5 (± 21.6)		

Notes:

[15] - PRO analysis set with available data at each time point

[16] - PRO analysis set with available data at each time point

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From first dose of any study drug up to 30 days after last dose; median duration was 338 days for placebo and 251 days for trebananib,

Adverse event reporting additional description:

A total of 336 subjects in the placebo group and 675 subjects in the trebananib group received ≥ 1 dose of study treatment and were included in the safety analysis set (1 subject randomized to the placebo group received trebananib and was included in the trebananib group for safety analysis).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.1

Reporting groups

Reporting group title	Trebananib + Paclitaxel + Carboplatin

Reporting group description:

Participants received trebananib 15 mg/kg IV once a week, paclitaxel 175 mg/m² infusion Q3W, and carboplatin AUC 5 or 6 IV Q3W for 6 cycles followed by trebananib 15 mg/kg IV once a week maintenance for 18 months.

Reporting group title	Placebo + Paclitaxel + Carboplatin

Reporting group description:

Participants received placebo intravenous (IV) infusion once a week, paclitaxel 175 mg/m² by IV infusion once every 3 weeks (Q3W), and carboplatin at an area under the curve (AUC) 5 or 6 IV Q3W for 6 cycles followed by placebo IV once a week maintenance for 18 months.

Serious adverse events	Trebananib + Paclitaxel + Carboplatin	Placebo + Paclitaxel + Carboplatin	
Total subjects affected by serious adverse events			
subjects affected / exposed	269 / 675 (39.85%)	104 / 336 (30.95%)	
number of deaths (all causes)	266	135	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer stage i			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endometrial cancer stage i			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Invasive ductal breast carcinoma			

subjects affected / exposed	3 / 675 (0.44%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malignant melanoma in situ			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malignant neoplasm of pleura			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malignant pleural effusion			
subjects affected / exposed	1 / 675 (0.15%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastases to central nervous system			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastases to liver			
subjects affected / exposed	1 / 675 (0.15%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mycosis fungoides			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ovarian cancer			
subjects affected / exposed	1 / 675 (0.15%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Paraneoplastic syndrome			

subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Arterial thrombosis			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Capillary leak syndrome			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Deep vein thrombosis			
subjects affected / exposed	3 / 675 (0.44%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	2 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertension			
subjects affected / exposed	4 / 675 (0.59%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	2 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypotension			
subjects affected / exposed	1 / 675 (0.15%)	2 / 336 (0.60%)	
occurrences causally related to treatment / all	0 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Jugular vein thrombosis			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphocele			
subjects affected / exposed	6 / 675 (0.89%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 8	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphoedema			

subjects affected / exposed	5 / 675 (0.74%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	2 / 5	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Shock			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombophlebitis superficial			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombosis			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	5 / 675 (0.74%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	1 / 5	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest pain			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chills			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Facial pain			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fatigue			

subjects affected / exposed	6 / 675 (0.89%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	3 / 6	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General physical health deterioration			
subjects affected / exposed	7 / 675 (1.04%)	3 / 336 (0.89%)	
occurrences causally related to treatment / all	2 / 11	0 / 3	
deaths causally related to treatment / all	0 / 4	0 / 0	
Generalised oedema			
subjects affected / exposed	5 / 675 (0.74%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	3 / 5	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Impaired healing			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Incarcerated hernia			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Localised oedema			
subjects affected / exposed	7 / 675 (1.04%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	5 / 7	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malaise			
subjects affected / exposed	2 / 675 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple organ dysfunction syndrome			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Non-cardiac chest pain			

subjects affected / exposed	1 / 675 (0.15%)	3 / 336 (0.89%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	10 / 675 (1.48%)	9 / 336 (2.68%)	
occurrences causally related to treatment / all	0 / 12	0 / 12	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sudden death			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypersensitivity			
subjects affected / exposed	3 / 675 (0.44%)	2 / 336 (0.60%)	
occurrences causally related to treatment / all	0 / 4	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Female genital tract fistula			
subjects affected / exposed	2 / 675 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vaginal discharge			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			

subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Apnoeic attack			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aspiration			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			
subjects affected / exposed	7 / 675 (1.04%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 7	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea at rest			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea exertional			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoxia			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			
subjects affected / exposed	24 / 675 (3.56%)	3 / 336 (0.89%)	
occurrences causally related to treatment / all	10 / 28	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary artery thrombosis			

subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	10 / 675 (1.48%)	3 / 336 (0.89%)	
occurrences causally related to treatment / all	4 / 10	1 / 3	
deaths causally related to treatment / all	0 / 1	0 / 0	
Respiratory failure			
subjects affected / exposed	2 / 675 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Psychiatric disorders			
Completed suicide			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Confusional state			
subjects affected / exposed	2 / 675 (0.30%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Depression			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suicidal ideation			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Blood creatinine increased			
subjects affected / exposed	2 / 675 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 6	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood culture positive			

subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood sodium decreased			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Computerised tomogram thorax abnormal			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Culture urine positive			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General physical condition abnormal			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liver function test increased			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutrophil count decreased			
subjects affected / exposed	2 / 675 (0.30%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 7	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Platelet count decreased			
subjects affected / exposed	3 / 675 (0.44%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	1 / 3	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
White blood cell count increased			

subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Abdominal wound dehiscence			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Craniocerebral injury			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femoral neck fracture			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (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	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fibula fracture			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal anastomotic leak			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hip fracture			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Humerus fracture			

subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infusion related reaction			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Joint dislocation			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscle strain			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post-traumatic pain			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
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	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ureteric injury			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular access site thrombosis			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound complication			

subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound dehiscence			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound evisceration			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute coronary syndrome			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina pectoris			
subjects affected / exposed	2 / 675 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina unstable			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			
subjects affected / exposed	3 / 675 (0.44%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 3	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial flutter			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac arrest			

subjects affected / exposed	2 / 675 (0.30%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 2	1 / 1	
deaths causally related to treatment / all	0 / 2	0 / 0	
Cardiac failure			
subjects affected / exposed	2 / 675 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			
subjects affected / exposed	1 / 675 (0.15%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Palpitations			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericardial effusion			
subjects affected / exposed	2 / 675 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinus node dysfunction			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinus tachycardia			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
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 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Ataxia			

subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral haemorrhage			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral ischaemia			
subjects affected / exposed	2 / 675 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrovascular accident			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Depressed level of consciousness			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dizziness			
subjects affected / exposed	3 / 675 (0.44%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	1 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hemiparesis			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral motor neuropathy			
subjects affected / exposed	1 / 675 (0.15%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral sensory neuropathy			

subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seizure			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seizure like phenomena			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	4 / 675 (0.59%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	2 / 5	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient ischaemic attack			
subjects affected / exposed	2 / 675 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tremor			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	6 / 675 (0.89%)	4 / 336 (1.19%)	
occurrences causally related to treatment / all	3 / 6	1 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Disseminated intravascular coagulation			
subjects affected / exposed	2 / 675 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Febrile neutropenia			

subjects affected / exposed	14 / 675 (2.07%)	4 / 336 (1.19%)	
occurrences causally related to treatment / all	5 / 16	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhagic disorder			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Leukopenia			
subjects affected / exposed	6 / 675 (0.89%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 6	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphadenopathy			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (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	17 / 675 (2.52%)	15 / 336 (4.46%)	
occurrences causally related to treatment / all	0 / 18	2 / 17	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancytopenia			
subjects affected / exposed	2 / 675 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Splenic haemorrhage			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			
subjects affected / exposed	6 / 675 (0.89%)	2 / 336 (0.60%)	
occurrences causally related to treatment / all	1 / 8	1 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Deafness unilateral			

subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tinnitus			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vestibular disorder			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Conjunctival oedema			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diplopia			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Glaucoma			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Photopsia			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Visual impairment			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vitreous floaters			

subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	1 / 675 (0.15%)	2 / 336 (0.60%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain			
subjects affected / exposed	20 / 675 (2.96%)	9 / 336 (2.68%)	
occurrences causally related to treatment / all	1 / 21	2 / 11	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain lower			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (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	2 / 675 (0.30%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal strangulated hernia			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ascites			
subjects affected / exposed	26 / 675 (3.85%)	6 / 336 (1.79%)	
occurrences causally related to treatment / all	14 / 38	1 / 7	
deaths causally related to treatment / all	0 / 1	0 / 0	
Colitis			
subjects affected / exposed	2 / 675 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Constipation			

subjects affected / exposed	10 / 675 (1.48%)	2 / 336 (0.60%)	
occurrences causally related to treatment / all	1 / 10	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	8 / 675 (1.19%)	3 / 336 (0.89%)	
occurrences causally related to treatment / all	2 / 9	3 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenal perforation			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspepsia			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterocolitis			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric ulcer			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric volvulus			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastritis			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorder			

subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal obstruction			
subjects affected / exposed	2 / 675 (0.30%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhoids			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (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	10 / 675 (1.48%)	2 / 336 (0.60%)	
occurrences causally related to treatment / all	2 / 14	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal haematoma			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal obstruction			
subjects affected / exposed	9 / 675 (1.33%)	7 / 336 (2.08%)	
occurrences causally related to treatment / all	1 / 10	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal perforation			
subjects affected / exposed	2 / 675 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal prolapse			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intra-abdominal haemorrhage			

subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestinal obstruction			
subjects affected / exposed	2 / 675 (0.30%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestine perforation			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mesenteric vein thrombosis			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			
subjects affected / exposed	9 / 675 (1.33%)	4 / 336 (1.19%)	
occurrences causally related to treatment / all	3 / 12	1 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenic colitis			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Oesophageal haemorrhage			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritoneal haemorrhage			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumoperitoneum			

subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal obstruction			
subjects affected / exposed	12 / 675 (1.78%)	7 / 336 (2.08%)	
occurrences causally related to treatment / all	1 / 12	0 / 7	
deaths causally related to treatment / all	0 / 1	0 / 0	
Stomatitis			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subileus			
subjects affected / exposed	13 / 675 (1.93%)	6 / 336 (1.79%)	
occurrences causally related to treatment / all	1 / 18	2 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	12 / 675 (1.78%)	7 / 336 (2.08%)	
occurrences causally related to treatment / all	2 / 17	1 / 9	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Bile duct stone			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis			
subjects affected / exposed	1 / 675 (0.15%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholestasis			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic failure			

subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Erythema multiforme			
subjects affected / exposed	1 / 675 (0.15%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	3 / 675 (0.44%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematuria			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hydronephrosis			
subjects affected / exposed	2 / 675 (0.30%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Obstructive uropathy			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal failure			
subjects affected / exposed	2 / 675 (0.30%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary bladder rupture			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary retention			

subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract obstruction			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chondrocalcinosis			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Flank pain			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral disc protrusion			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscular weakness			
subjects affected / exposed	2 / 675 (0.30%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	1 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Abdominal abscess			
subjects affected / exposed	1 / 675 (0.15%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Abdominal infection			
subjects affected / exposed	1 / 675 (0.15%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abscess limb			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacteraemia			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacterial infection			
subjects affected / exposed	2 / 675 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	1 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	3 / 675 (0.44%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium colitis			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium difficile colitis			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colonic abscess			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cystitis			

subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device related infection			
subjects affected / exposed	3 / 675 (0.44%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia sepsis			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes zoster			
subjects affected / exposed	1 / 675 (0.15%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infected lymphocele			
subjects affected / exposed	4 / 675 (0.59%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 6	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infective spondylitis			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Kidney infection			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection			

subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung infection			
subjects affected / exposed	2 / 675 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	2 / 3	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Mastitis			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pelvic abscess			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritoneal abscess			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pharyngitis			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	5 / 675 (0.74%)	3 / 336 (0.89%)	
occurrences causally related to treatment / all	1 / 6	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural infection			
subjects affected / exposed	2 / 675 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Postoperative wound infection			

subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pseudomonas infection			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis			
subjects affected / exposed	2 / 675 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis acute			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	2 / 675 (0.30%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis syndrome			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic shock			
subjects affected / exposed	2 / 675 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal sepsis			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tooth abscess			

subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection			
subjects affected / exposed	3 / 675 (0.44%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	6 / 675 (0.89%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	1 / 6	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection bacterial			
subjects affected / exposed	2 / 675 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	8 / 675 (1.19%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	4 / 11	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dehydration			
subjects affected / exposed	6 / 675 (0.89%)	6 / 336 (1.79%)	
occurrences causally related to treatment / all	2 / 10	1 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperglycaemia			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperkalaemia			
subjects affected / exposed	2 / 675 (0.30%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoalbuminaemia			

subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypocalcaemia			
subjects affected / exposed	1 / 675 (0.15%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 1	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoglycaemia			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypokalaemia			
subjects affected / exposed	4 / 675 (0.59%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 4	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypomagnesaemia			
subjects affected / exposed	1 / 675 (0.15%)	1 / 336 (0.30%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyponatraemia			
subjects affected / exposed	5 / 675 (0.74%)	0 / 336 (0.00%)	
occurrences causally related to treatment / all	1 / 5	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Trebananib + Paclitaxel + Carboplatin	Placebo + Paclitaxel + Carboplatin	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	664 / 675 (98.37%)	326 / 336 (97.02%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Benign neoplasm			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	

Benign neoplasm of thyroid gland			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Breast cancer			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Cancer pain			
subjects affected / exposed	2 / 675 (0.30%)	0 / 336 (0.00%)	
occurrences (all)	2	0	
Endometrial adenocarcinoma			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Lung adenocarcinoma			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Lung neoplasm malignant			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Malignant ascites			
subjects affected / exposed	2 / 675 (0.30%)	0 / 336 (0.00%)	
occurrences (all)	2	0	
Malignant pleural effusion			
subjects affected / exposed	2 / 675 (0.30%)	0 / 336 (0.00%)	
occurrences (all)	2	0	
Metastases to lymph nodes			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Neoplasm			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Pancreatic neoplasm			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Respiratory papilloma			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	

Seborrhoeic keratosis			
subjects affected / exposed	2 / 675 (0.30%)	0 / 336 (0.00%)	
occurrences (all)	2	0	
Skin papilloma			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Squamous cell carcinoma			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Tumour haemorrhage			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Tumour pain			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Vascular disorders			
Bloody discharge			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Deep vein thrombosis			
subjects affected / exposed	14 / 675 (2.07%)	2 / 336 (0.60%)	
occurrences (all)	16	2	
Diastolic hypertension			
subjects affected / exposed	1 / 675 (0.15%)	1 / 336 (0.30%)	
occurrences (all)	1	1	
Embolism			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Extremity necrosis			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Flushing			
subjects affected / exposed	21 / 675 (3.11%)	11 / 336 (3.27%)	
occurrences (all)	27	11	
Haematoma			

subjects affected / exposed	5 / 675 (0.74%)	6 / 336 (1.79%)	
occurrences (all)	5	7	
Haemorrhage			
subjects affected / exposed	3 / 675 (0.44%)	0 / 336 (0.00%)	
occurrences (all)	3	0	
Hot flush			
subjects affected / exposed	41 / 675 (6.07%)	22 / 336 (6.55%)	
occurrences (all)	60	26	
Hyperaemia			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	2	0	
Hypertension			
subjects affected / exposed	61 / 675 (9.04%)	27 / 336 (8.04%)	
occurrences (all)	89	38	
Hypotension			
subjects affected / exposed	26 / 675 (3.85%)	10 / 336 (2.98%)	
occurrences (all)	28	13	
Jugular vein thrombosis			
subjects affected / exposed	3 / 675 (0.44%)	0 / 336 (0.00%)	
occurrences (all)	3	0	
Lymphocele			
subjects affected / exposed	6 / 675 (0.89%)	6 / 336 (1.79%)	
occurrences (all)	6	7	
Lymphoedema			
subjects affected / exposed	79 / 675 (11.70%)	11 / 336 (3.27%)	
occurrences (all)	130	17	
Lymphorrhoea			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Microangiopathy			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Orthostatic hypotension			
subjects affected / exposed	12 / 675 (1.78%)	4 / 336 (1.19%)	
occurrences (all)	14	6	
Pallor			

subjects affected / exposed	2 / 675 (0.30%)	2 / 336 (0.60%)	
occurrences (all)	2	4	
Peripheral coldness			
subjects affected / exposed	1 / 675 (0.15%)	2 / 336 (0.60%)	
occurrences (all)	1	2	
Peripheral ischaemia			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Peripheral venous disease			
subjects affected / exposed	4 / 675 (0.59%)	2 / 336 (0.60%)	
occurrences (all)	4	2	
Phlebitis			
subjects affected / exposed	4 / 675 (0.59%)	1 / 336 (0.30%)	
occurrences (all)	8	1	
Phlebitis superficial			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Raynaud's phenomenon			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Thrombophlebitis			
subjects affected / exposed	2 / 675 (0.30%)	1 / 336 (0.30%)	
occurrences (all)	2	1	
Thrombophlebitis superficial			
subjects affected / exposed	3 / 675 (0.44%)	0 / 336 (0.00%)	
occurrences (all)	3	0	
Thrombosis			
subjects affected / exposed	6 / 675 (0.89%)	1 / 336 (0.30%)	
occurrences (all)	6	1	
Varicose vein			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Vascular pain			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Vascular rupture			

subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Venous thrombosis			
subjects affected / exposed	4 / 675 (0.59%)	2 / 336 (0.60%)	
occurrences (all)	4	2	
Venous thrombosis limb			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
Adverse drug reaction			
subjects affected / exposed	1 / 675 (0.15%)	3 / 336 (0.89%)	
occurrences (all)	1	3	
Application site pain			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Application site rash			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Application site reaction			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Asthenia			
subjects affected / exposed	117 / 675 (17.33%)	70 / 336 (20.83%)	
occurrences (all)	249	148	
Axillary pain			
subjects affected / exposed	1 / 675 (0.15%)	2 / 336 (0.60%)	
occurrences (all)	1	2	
Catheter site bruise			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Catheter site dermatitis			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Catheter site erosion			

subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Catheter site erythema			
subjects affected / exposed	2 / 675 (0.30%)	1 / 336 (0.30%)	
occurrences (all)	3	1	
Catheter site extravasation			
subjects affected / exposed	2 / 675 (0.30%)	0 / 336 (0.00%)	
occurrences (all)	2	0	
Catheter site haematoma			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Catheter site inflammation			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Catheter site necrosis			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Catheter site pain			
subjects affected / exposed	5 / 675 (0.74%)	5 / 336 (1.49%)	
occurrences (all)	5	5	
Catheter site rash			
subjects affected / exposed	1 / 675 (0.15%)	2 / 336 (0.60%)	
occurrences (all)	1	3	
Catheter site related reaction			
subjects affected / exposed	0 / 675 (0.00%)	2 / 336 (0.60%)	
occurrences (all)	0	2	
Catheter site ulcer			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Catheter site vesicles			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Chest discomfort			
subjects affected / exposed	10 / 675 (1.48%)	4 / 336 (1.19%)	
occurrences (all)	11	4	
Chest pain			

subjects affected / exposed	23 / 675 (3.41%)	19 / 336 (5.65%)	
occurrences (all)	30	20	
Chills			
subjects affected / exposed	13 / 675 (1.93%)	7 / 336 (2.08%)	
occurrences (all)	16	10	
Complication associated with device			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Cyst			
subjects affected / exposed	5 / 675 (0.74%)	0 / 336 (0.00%)	
occurrences (all)	6	0	
Decreased activity			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Discomfort			
subjects affected / exposed	4 / 675 (0.59%)	2 / 336 (0.60%)	
occurrences (all)	4	2	
Disease progression			
subjects affected / exposed	1 / 675 (0.15%)	1 / 336 (0.30%)	
occurrences (all)	1	1	
Early satiety			
subjects affected / exposed	3 / 675 (0.44%)	1 / 336 (0.30%)	
occurrences (all)	3	1	
Facial pain			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Extravasation			
subjects affected / exposed	2 / 675 (0.30%)	2 / 336 (0.60%)	
occurrences (all)	2	2	
Fatigue			
subjects affected / exposed	302 / 675 (44.74%)	139 / 336 (41.37%)	
occurrences (all)	671	293	
Feeling cold			
subjects affected / exposed	4 / 675 (0.59%)	1 / 336 (0.30%)	
occurrences (all)	4	2	
Gait disturbance			

subjects affected / exposed	6 / 675 (0.89%)	2 / 336 (0.60%)	
occurrences (all)	6	2	
Feeling hot			
subjects affected / exposed	3 / 675 (0.44%)	3 / 336 (0.89%)	
occurrences (all)	6	4	
General physical health deterioration			
subjects affected / exposed	9 / 675 (1.33%)	2 / 336 (0.60%)	
occurrences (all)	10	2	
Generalised oedema			
subjects affected / exposed	85 / 675 (12.59%)	9 / 336 (2.68%)	
occurrences (all)	123	11	
Hernia			
subjects affected / exposed	2 / 675 (0.30%)	5 / 336 (1.49%)	
occurrences (all)	2	6	
Impaired healing			
subjects affected / exposed	2 / 675 (0.30%)	1 / 336 (0.30%)	
occurrences (all)	2	1	
Hyperthermia			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Inflammation			
subjects affected / exposed	2 / 675 (0.30%)	0 / 336 (0.00%)	
occurrences (all)	2	0	
Induration			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Influenza like illness			
subjects affected / exposed	22 / 675 (3.26%)	14 / 336 (4.17%)	
occurrences (all)	28	17	
Infusion site bruising			
subjects affected / exposed	1 / 675 (0.15%)	1 / 336 (0.30%)	
occurrences (all)	1	1	
Infusion site erythema			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Infusion site extravasation			

subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Infusion site oedema			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Infusion site pain			
subjects affected / exposed	1 / 675 (0.15%)	3 / 336 (0.89%)	
occurrences (all)	1	3	
Infusion site pruritus			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Infusion site reaction			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Injection site bruising			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Injection site extravasation			
subjects affected / exposed	2 / 675 (0.30%)	0 / 336 (0.00%)	
occurrences (all)	3	0	
Injection site pain			
subjects affected / exposed	1 / 675 (0.15%)	1 / 336 (0.30%)	
occurrences (all)	1	1	
Injection site phlebitis			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	2	0	
Injection site reaction			
subjects affected / exposed	3 / 675 (0.44%)	0 / 336 (0.00%)	
occurrences (all)	3	0	
Localised oedema			
subjects affected / exposed	367 / 675 (54.37%)	86 / 336 (25.60%)	
occurrences (all)	855	132	
Malaise			
subjects affected / exposed	13 / 675 (1.93%)	11 / 336 (3.27%)	
occurrences (all)	13	14	
Mass			

subjects affected / exposed	2 / 675 (0.30%)	0 / 336 (0.00%)	
occurrences (all)	2	0	
Mucosal dryness			
subjects affected / exposed	1 / 675 (0.15%)	2 / 336 (0.60%)	
occurrences (all)	1	2	
Mucosal inflammation			
subjects affected / exposed	33 / 675 (4.89%)	11 / 336 (3.27%)	
occurrences (all)	47	14	
Mucous membrane disorder			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Non-cardiac chest pain			
subjects affected / exposed	6 / 675 (0.89%)	2 / 336 (0.60%)	
occurrences (all)	6	3	
Pain			
subjects affected / exposed	73 / 675 (10.81%)	33 / 336 (9.82%)	
occurrences (all)	94	45	
Peripheral swelling			
subjects affected / exposed	2 / 675 (0.30%)	0 / 336 (0.00%)	
occurrences (all)	2	0	
Polyp			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Pyrexia			
subjects affected / exposed	65 / 675 (9.63%)	40 / 336 (11.90%)	
occurrences (all)	75	54	
Sensation of foreign body			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Suprapubic pain			
subjects affected / exposed	2 / 675 (0.30%)	0 / 336 (0.00%)	
occurrences (all)	2	0	
Swelling			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Temperature intolerance			

subjects affected / exposed	0 / 675 (0.00%)	2 / 336 (0.60%)	
occurrences (all)	0	2	
Tenderness			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Thirst			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Thirst decreased			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Vascular complication associated with device			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Immune system disorders			
Contrast media allergy			
subjects affected / exposed	1 / 675 (0.15%)	2 / 336 (0.60%)	
occurrences (all)	1	2	
Anaphylactic reaction			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Drug hypersensitivity			
subjects affected / exposed	12 / 675 (1.78%)	14 / 336 (4.17%)	
occurrences (all)	15	16	
Cytokine release syndrome			
subjects affected / exposed	0 / 675 (0.00%)	2 / 336 (0.60%)	
occurrences (all)	0	2	
Food allergy			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Hypersensitivity			
subjects affected / exposed	40 / 675 (5.93%)	16 / 336 (4.76%)	
occurrences (all)	49	19	
Seasonal allergy			

subjects affected / exposed	4 / 675 (0.59%)	2 / 336 (0.60%)	
occurrences (all)	4	3	
Sarcoidosis			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Social circumstances			
Menopause			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Reproductive system and breast disorders			
Atrophic vulvovaginitis			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Bartholin's cyst			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Bleeding anovulatory			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Breast cyst			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Breast disorder			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Breast hyperplasia			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Breast mass			
subjects affected / exposed	3 / 675 (0.44%)	0 / 336 (0.00%)	
occurrences (all)	3	0	
Breast pain			
subjects affected / exposed	5 / 675 (0.74%)	3 / 336 (0.89%)	
occurrences (all)	7	3	
Breast tenderness			

subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Cervical dysplasia			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Cervix disorder			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Cervix erythema			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Cystocele			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Dyspareunia			
subjects affected / exposed	4 / 675 (0.59%)	1 / 336 (0.30%)	
occurrences (all)	4	1	
Female genital tract fistula			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Galactorrhoea			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Genital discharge			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Genital pain			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Genital rash			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Menopausal symptoms			
subjects affected / exposed	0 / 675 (0.00%)	4 / 336 (1.19%)	
occurrences (all)	0	4	
Menorrhagia			

subjects affected / exposed	1 / 675 (0.15%)	1 / 336 (0.30%)	
occurrences (all)	1	1	
Metrorrhagia			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Pelvic discomfort			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Pelvic fluid collection			
subjects affected / exposed	3 / 675 (0.44%)	0 / 336 (0.00%)	
occurrences (all)	3	0	
Pelvic pain			
subjects affected / exposed	10 / 675 (1.48%)	6 / 336 (1.79%)	
occurrences (all)	11	7	
Perineal ulceration			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Pruritus genital			
subjects affected / exposed	1 / 675 (0.15%)	1 / 336 (0.30%)	
occurrences (all)	1	1	
Retracted nipple			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Vaginal discharge			
subjects affected / exposed	11 / 675 (1.63%)	6 / 336 (1.79%)	
occurrences (all)	13	6	
Vaginal haemorrhage			
subjects affected / exposed	8 / 675 (1.19%)	9 / 336 (2.68%)	
occurrences (all)	8	9	
Vaginal inflammation			
subjects affected / exposed	1 / 675 (0.15%)	1 / 336 (0.30%)	
occurrences (all)	1	1	
Vaginal odour			
subjects affected / exposed	2 / 675 (0.30%)	0 / 336 (0.00%)	
occurrences (all)	2	0	
Vulva cyst			

subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	2	0	
Vulvovaginal discomfort			
subjects affected / exposed	2 / 675 (0.30%)	1 / 336 (0.30%)	
occurrences (all)	2	1	
Vulvovaginal dryness			
subjects affected / exposed	5 / 675 (0.74%)	1 / 336 (0.30%)	
occurrences (all)	5	1	
Vulvovaginal pruritus			
subjects affected / exposed	3 / 675 (0.44%)	1 / 336 (0.30%)	
occurrences (all)	3	1	
Respiratory, thoracic and mediastinal disorders			
Acquired diaphragmatic eventration			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Anoxia			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Aspiration			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Asthma			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Atelectasis			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Catarrh			
subjects affected / exposed	6 / 675 (0.89%)	2 / 336 (0.60%)	
occurrences (all)	7	3	
Cough			
subjects affected / exposed	99 / 675 (14.67%)	49 / 336 (14.58%)	
occurrences (all)	125	63	
Cough decreased			

subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Dry throat			
subjects affected / exposed	1 / 675 (0.15%)	1 / 336 (0.30%)	
occurrences (all)	1	1	
Dysphonia			
subjects affected / exposed	6 / 675 (0.89%)	7 / 336 (2.08%)	
occurrences (all)	6	8	
Dyspnoea			
subjects affected / exposed	115 / 675 (17.04%)	39 / 336 (11.61%)	
occurrences (all)	166	49	
Dyspnoea at rest			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Dyspnoea exertional			
subjects affected / exposed	35 / 675 (5.19%)	12 / 336 (3.57%)	
occurrences (all)	43	14	
Emphysema			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Epistaxis			
subjects affected / exposed	23 / 675 (3.41%)	16 / 336 (4.76%)	
occurrences (all)	24	18	
Haemoptysis			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Hiccups			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Hydrothorax			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Hyperventilation			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Hypoxia			

subjects affected / exposed	3 / 675 (0.44%)	0 / 336 (0.00%)	
occurrences (all)	3	0	
Increased bronchial secretion			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	2	0	
Increased upper airway secretion			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Laryngeal inflammation			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	2	
Laryngeal pain			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Lung infiltration			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Nasal congestion			
subjects affected / exposed	13 / 675 (1.93%)	5 / 336 (1.49%)	
occurrences (all)	22	8	
Nasal discomfort			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Nasal dryness			
subjects affected / exposed	5 / 675 (0.74%)	0 / 336 (0.00%)	
occurrences (all)	5	0	
Nasal mucosal disorder			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Nasal ulcer			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Oropharyngeal discomfort			
subjects affected / exposed	1 / 675 (0.15%)	1 / 336 (0.30%)	
occurrences (all)	1	1	
Oropharyngeal pain			

subjects affected / exposed	44 / 675 (6.52%)	22 / 336 (6.55%)	
occurrences (all)	49	28	
Paranasal sinus hypersecretion			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Pharyngeal inflammation			
subjects affected / exposed	1 / 675 (0.15%)	1 / 336 (0.30%)	
occurrences (all)	1	1	
Pleural disorder			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Pleural effusion			
subjects affected / exposed	59 / 675 (8.74%)	7 / 336 (2.08%)	
occurrences (all)	76	9	
Pleuritic pain			
subjects affected / exposed	1 / 675 (0.15%)	3 / 336 (0.89%)	
occurrences (all)	1	3	
Pneumothorax			
subjects affected / exposed	1 / 675 (0.15%)	1 / 336 (0.30%)	
occurrences (all)	1	1	
Productive cough			
subjects affected / exposed	15 / 675 (2.22%)	8 / 336 (2.38%)	
occurrences (all)	16	8	
Pulmonary congestion			
subjects affected / exposed	2 / 675 (0.30%)	0 / 336 (0.00%)	
occurrences (all)	2	0	
Pulmonary embolism			
subjects affected / exposed	1 / 675 (0.15%)	4 / 336 (1.19%)	
occurrences (all)	1	4	
Pulmonary hypertension			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Pulmonary oedema			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Rales			

subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Reflux laryngitis			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Respiratory depression			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Respiratory disorder			
subjects affected / exposed	1 / 675 (0.15%)	1 / 336 (0.30%)	
occurrences (all)	1	1	
Respiratory tract congestion			
subjects affected / exposed	3 / 675 (0.44%)	2 / 336 (0.60%)	
occurrences (all)	3	2	
Rhinitis allergic			
subjects affected / exposed	13 / 675 (1.93%)	3 / 336 (0.89%)	
occurrences (all)	16	3	
Rhinitis perennial			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Rhinorrhoea			
subjects affected / exposed	30 / 675 (4.44%)	8 / 336 (2.38%)	
occurrences (all)	31	9	
Sinus congestion			
subjects affected / exposed	6 / 675 (0.89%)	2 / 336 (0.60%)	
occurrences (all)	6	2	
Sinus disorder			
subjects affected / exposed	1 / 675 (0.15%)	1 / 336 (0.30%)	
occurrences (all)	1	1	
Sinusitis noninfective			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Sinus pain			
subjects affected / exposed	2 / 675 (0.30%)	2 / 336 (0.60%)	
occurrences (all)	2	2	
Sneezing			

subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Sputum discoloured			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Throat irritation			
subjects affected / exposed	7 / 675 (1.04%)	0 / 336 (0.00%)	
occurrences (all)	8	0	
Tachypnoea			
subjects affected / exposed	1 / 675 (0.15%)	1 / 336 (0.30%)	
occurrences (all)	1	1	
Upper respiratory tract inflammation			
subjects affected / exposed	2 / 675 (0.30%)	0 / 336 (0.00%)	
occurrences (all)	6	0	
Upper-airway cough syndrome			
subjects affected / exposed	8 / 675 (1.19%)	5 / 336 (1.49%)	
occurrences (all)	8	6	
Psychiatric disorders			
Adjustment disorder			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Adjustment disorder with depressed mood			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Affect lability			
subjects affected / exposed	2 / 675 (0.30%)	0 / 336 (0.00%)	
occurrences (all)	2	0	
Agitation			
subjects affected / exposed	3 / 675 (0.44%)	1 / 336 (0.30%)	
occurrences (all)	3	3	
Anxiety			
subjects affected / exposed	50 / 675 (7.41%)	31 / 336 (9.23%)	
occurrences (all)	56	40	
Anxiety disorder due to a general medical condition			

subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Apathy			
subjects affected / exposed	1 / 675 (0.15%)	1 / 336 (0.30%)	
occurrences (all)	1	2	
Confusional state			
subjects affected / exposed	4 / 675 (0.59%)	1 / 336 (0.30%)	
occurrences (all)	5	1	
Delirium			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Depressed mood			
subjects affected / exposed	6 / 675 (0.89%)	6 / 336 (1.79%)	
occurrences (all)	6	6	
Depression			
subjects affected / exposed	35 / 675 (5.19%)	20 / 336 (5.95%)	
occurrences (all)	42	26	
Fear			
subjects affected / exposed	2 / 675 (0.30%)	0 / 336 (0.00%)	
occurrences (all)	2	0	
Hallucination			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Illusion			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Insomnia			
subjects affected / exposed	103 / 675 (15.26%)	55 / 336 (16.37%)	
occurrences (all)	137	76	
Insomnia related to another mental condition			
subjects affected / exposed	1 / 675 (0.15%)	1 / 336 (0.30%)	
occurrences (all)	2	1	
Irritability			
subjects affected / exposed	1 / 675 (0.15%)	1 / 336 (0.30%)	
occurrences (all)	1	1	

Libido decreased			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Major depression			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Mental disorder			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Mental status changes			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Mood altered			
subjects affected / exposed	2 / 675 (0.30%)	3 / 336 (0.89%)	
occurrences (all)	2	5	
Mood swings			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Nervousness			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Nightmare			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Panic attack			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Restlessness			
subjects affected / exposed	3 / 675 (0.44%)	3 / 336 (0.89%)	
occurrences (all)	6	5	
Sleep disorder			
subjects affected / exposed	2 / 675 (0.30%)	5 / 336 (1.49%)	
occurrences (all)	2	6	
Stress			
subjects affected / exposed	2 / 675 (0.30%)	0 / 336 (0.00%)	
occurrences (all)	2	0	

Suicidal ideation			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Tearfulness			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Product issues			
Device failure			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Device issue			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Device occlusion			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Thrombosis in device			
subjects affected / exposed	1 / 675 (0.15%)	1 / 336 (0.30%)	
occurrences (all)	1	1	
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Drug-induced liver injury			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Hepatic function abnormal			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	3	0	
Hepatic pain			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Hepatic steatosis			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Hepatic vein thrombosis			

subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Hepatotoxicity			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Hyperbilirubinaemia			
subjects affected / exposed	5 / 675 (0.74%)	1 / 336 (0.30%)	
occurrences (all)	6	2	
Hypertransaminasaemia			
subjects affected / exposed	3 / 675 (0.44%)	5 / 336 (1.49%)	
occurrences (all)	4	12	
Investigations			
Activated partial thromboplastin time abnormal			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Activated partial thromboplastin time prolonged			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Alanine aminotransferase increased			
subjects affected / exposed	31 / 675 (4.59%)	20 / 336 (5.95%)	
occurrences (all)	68	27	
Amylase increased			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	3	0	
Aspartate aminotransferase increased			
subjects affected / exposed	22 / 675 (3.26%)	15 / 336 (4.46%)	
occurrences (all)	43	21	
Bacterial test			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Bilirubin conjugated increased			
subjects affected / exposed	2 / 675 (0.30%)	0 / 336 (0.00%)	
occurrences (all)	2	0	
Bleeding time prolonged			

subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Blood albumin abnormal			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Blood albumin decreased			
subjects affected / exposed	5 / 675 (0.74%)	0 / 336 (0.00%)	
occurrences (all)	6	0	
Blood alkaline phosphatase increased			
subjects affected / exposed	13 / 675 (1.93%)	10 / 336 (2.98%)	
occurrences (all)	14	12	
Blood bilirubin increased			
subjects affected / exposed	4 / 675 (0.59%)	0 / 336 (0.00%)	
occurrences (all)	7	0	
Blood calcium decreased			
subjects affected / exposed	4 / 675 (0.59%)	1 / 336 (0.30%)	
occurrences (all)	4	1	
Blood cholesterol increased			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Blood creatine increased			
subjects affected / exposed	4 / 675 (0.59%)	4 / 336 (1.19%)	
occurrences (all)	4	6	
Blood creatinine abnormal			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Blood creatinine increased			
subjects affected / exposed	19 / 675 (2.81%)	6 / 336 (1.79%)	
occurrences (all)	32	8	
Blood gases abnormal			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Blood glucose increased			
subjects affected / exposed	2 / 675 (0.30%)	3 / 336 (0.89%)	
occurrences (all)	2	6	
Blood lactate dehydrogenase			

increased			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Blood lactic acid increased			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Blood magnesium decreased			
subjects affected / exposed	10 / 675 (1.48%)	7 / 336 (2.08%)	
occurrences (all)	12	9	
Blood magnesium increased			
subjects affected / exposed	1 / 675 (0.15%)	1 / 336 (0.30%)	
occurrences (all)	1	1	
Blood parathyroid hormone increased			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Blood phosphorus decreased			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Blood phosphorus increased			
subjects affected / exposed	2 / 675 (0.30%)	1 / 336 (0.30%)	
occurrences (all)	4	1	
Blood potassium decreased			
subjects affected / exposed	4 / 675 (0.59%)	2 / 336 (0.60%)	
occurrences (all)	4	2	
Blood pressure decreased			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Blood pressure increased			
subjects affected / exposed	3 / 675 (0.44%)	1 / 336 (0.30%)	
occurrences (all)	9	1	
Blood sodium decreased			
subjects affected / exposed	1 / 675 (0.15%)	1 / 336 (0.30%)	
occurrences (all)	1	1	
Blood sodium increased			

subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Blood urea increased			
subjects affected / exposed	2 / 675 (0.30%)	1 / 336 (0.30%)	
occurrences (all)	2	1	
Blood uric acid abnormal			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Blood urine present			
subjects affected / exposed	2 / 675 (0.30%)	2 / 336 (0.60%)	
occurrences (all)	4	2	
C-reactive protein abnormal			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
C-reactive protein decreased			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
C-reactive protein increased			
subjects affected / exposed	1 / 675 (0.15%)	1 / 336 (0.30%)	
occurrences (all)	1	2	
Cardiac murmur			
subjects affected / exposed	3 / 675 (0.44%)	1 / 336 (0.30%)	
occurrences (all)	3	1	
Culture urine positive			
subjects affected / exposed	1 / 675 (0.15%)	1 / 336 (0.30%)	
occurrences (all)	1	1	
Echocardiogram abnormal			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Electrocardiogram abnormal			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	2	0	
Electrocardiogram t wave abnormal			
subjects affected / exposed	1 / 675 (0.15%)	1 / 336 (0.30%)	
occurrences (all)	1	1	
Fibrin d dimer increased			

subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Gamma-glutamyltransferase increased			
subjects affected / exposed	6 / 675 (0.89%)	2 / 336 (0.60%)	
occurrences (all)	10	2	
Glomerular filtration rate decreased			
subjects affected / exposed	3 / 675 (0.44%)	1 / 336 (0.30%)	
occurrences (all)	3	2	
Glucose urine			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Glycosylated haemoglobin increased			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Granulocyte count decreased			
subjects affected / exposed	2 / 675 (0.30%)	0 / 336 (0.00%)	
occurrences (all)	12	0	
Haematocrit decreased			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Haemoglobin			
subjects affected / exposed	8 / 675 (1.19%)	1 / 336 (0.30%)	
occurrences (all)	24	3	
Haemoglobin abnormal			
subjects affected / exposed	2 / 675 (0.30%)	1 / 336 (0.30%)	
occurrences (all)	2	1	
Haemoglobin decreased			
subjects affected / exposed	31 / 675 (4.59%)	9 / 336 (2.68%)	
occurrences (all)	73	18	
Heart rate decreased			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Heart rate increased			
subjects affected / exposed	1 / 675 (0.15%)	1 / 336 (0.30%)	
occurrences (all)	1	1	

Heart rate irregular			
subjects affected / exposed	1 / 675 (0.15%)	1 / 336 (0.30%)	
occurrences (all)	1	1	
Hepatic enzyme increased			
subjects affected / exposed	2 / 675 (0.30%)	2 / 336 (0.60%)	
occurrences (all)	4	2	
Hypophonesis			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
International normalised ratio increased			
subjects affected / exposed	3 / 675 (0.44%)	0 / 336 (0.00%)	
occurrences (all)	4	0	
Intraocular pressure increased			
subjects affected / exposed	4 / 675 (0.59%)	0 / 336 (0.00%)	
occurrences (all)	4	0	
Liver function test			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Liver function test increased			
subjects affected / exposed	1 / 675 (0.15%)	2 / 336 (0.60%)	
occurrences (all)	1	2	
Lymphocyte count decreased			
subjects affected / exposed	3 / 675 (0.44%)	1 / 336 (0.30%)	
occurrences (all)	7	6	
Nerve conduction studies abnormal			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Neutrophil count			
subjects affected / exposed	2 / 675 (0.30%)	2 / 336 (0.60%)	
occurrences (all)	2	2	
Neutrophil count abnormal			
subjects affected / exposed	0 / 675 (0.00%)	2 / 336 (0.60%)	
occurrences (all)	0	2	
Neutrophil count decreased			

subjects affected / exposed	46 / 675 (6.81%)	21 / 336 (6.25%)	
occurrences (all)	121	73	
Neutrophil count increased			
subjects affected / exposed	1 / 675 (0.15%)	1 / 336 (0.30%)	
occurrences (all)	1	1	
Nitrite urine present			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Pain assessment			
subjects affected / exposed	0 / 675 (0.00%)	2 / 336 (0.60%)	
occurrences (all)	0	3	
Platelet count decreased			
subjects affected / exposed	84 / 675 (12.44%)	34 / 336 (10.12%)	
occurrences (all)	263	86	
Platelet count increased			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Protein total			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Protein total abnormal			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Protein total decreased			
subjects affected / exposed	2 / 675 (0.30%)	1 / 336 (0.30%)	
occurrences (all)	2	1	
Protein urine			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Pulmonary physical examination abnormal			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Red blood cell count decreased			
subjects affected / exposed	3 / 675 (0.44%)	1 / 336 (0.30%)	
occurrences (all)	4	1	

Serum ferritin decreased			
subjects affected / exposed	1 / 675 (0.15%)	1 / 336 (0.30%)	
occurrences (all)	1	1	
Urine analysis abnormal			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	3	
Urine output decreased			
subjects affected / exposed	1 / 675 (0.15%)	2 / 336 (0.60%)	
occurrences (all)	1	2	
Urine output increased			
subjects affected / exposed	2 / 675 (0.30%)	0 / 336 (0.00%)	
occurrences (all)	2	0	
Urine protein, quantitative			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Vitamin d decreased			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Waist circumference increased			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Weight decreased			
subjects affected / exposed	28 / 675 (4.15%)	19 / 336 (5.65%)	
occurrences (all)	52	41	
Weight increased			
subjects affected / exposed	46 / 675 (6.81%)	19 / 336 (5.65%)	
occurrences (all)	107	27	
White blood cell analysis abnormal			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
White blood cell count			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
White blood cell count abnormal			
subjects affected / exposed	1 / 675 (0.15%)	1 / 336 (0.30%)	
occurrences (all)	1	1	

White blood cell count decreased			
subjects affected / exposed	48 / 675 (7.11%)	19 / 336 (5.65%)	
occurrences (all)	199	87	
White blood cell count increased			
subjects affected / exposed	2 / 675 (0.30%)	0 / 336 (0.00%)	
occurrences (all)	2	0	
White blood cells urine positive			
subjects affected / exposed	1 / 675 (0.15%)	1 / 336 (0.30%)	
occurrences (all)	1	1	
Injury, poisoning and procedural complications			
Animal scratch			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Arthropod bite			
subjects affected / exposed	1 / 675 (0.15%)	4 / 336 (1.19%)	
occurrences (all)	1	4	
Ankle fracture			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Arthropod sting			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Chest crushing			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Contusion			
subjects affected / exposed	16 / 675 (2.37%)	11 / 336 (3.27%)	
occurrences (all)	23	14	
Contrast media reaction			
subjects affected / exposed	2 / 675 (0.30%)	1 / 336 (0.30%)	
occurrences (all)	2	1	
Epicondylitis			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Craniocerebral injury			

subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Eye injury			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Excoriation			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Fall			
subjects affected / exposed	7 / 675 (1.04%)	1 / 336 (0.30%)	
occurrences (all)	12	2	
Foot fracture			
subjects affected / exposed	4 / 675 (0.59%)	1 / 336 (0.30%)	
occurrences (all)	5	1	
Foreign body			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Fracture			
subjects affected / exposed	1 / 675 (0.15%)	1 / 336 (0.30%)	
occurrences (all)	1	1	
Gastrointestinal disorder postoperative			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Gastrointestinal stoma complication			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Haematuria traumatic			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Hand fracture			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Head injury			
subjects affected / exposed	1 / 675 (0.15%)	1 / 336 (0.30%)	
occurrences (all)	1	1	

Hip fracture			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Humerus fracture			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Incision site erythema			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Incision site oedema			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Incision site pain			
subjects affected / exposed	7 / 675 (1.04%)	2 / 336 (0.60%)	
occurrences (all)	9	2	
Incisional hernia, obstructive			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Infusion related reaction			
subjects affected / exposed	21 / 675 (3.11%)	8 / 336 (2.38%)	
occurrences (all)	25	9	
Injury			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Laceration			
subjects affected / exposed	2 / 675 (0.30%)	1 / 336 (0.30%)	
occurrences (all)	3	1	
Ligament injury			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Ligament sprain			
subjects affected / exposed	2 / 675 (0.30%)	1 / 336 (0.30%)	
occurrences (all)	2	1	
Limb injury			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	

Meniscus injury			
subjects affected / exposed	1 / 675 (0.15%)	1 / 336 (0.30%)	
occurrences (all)	1	1	
Muscle strain			
subjects affected / exposed	1 / 675 (0.15%)	2 / 336 (0.60%)	
occurrences (all)	1	2	
Nerve injury			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Pneumothorax traumatic			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Post procedural complication			
subjects affected / exposed	4 / 675 (0.59%)	2 / 336 (0.60%)	
occurrences (all)	6	2	
Post procedural haematoma			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Post procedural haemorrhage			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Postoperative fever			
subjects affected / exposed	1 / 675 (0.15%)	1 / 336 (0.30%)	
occurrences (all)	1	1	
Postoperative hernia			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Postoperative ileus			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Postoperative wound complication			
subjects affected / exposed	1 / 675 (0.15%)	1 / 336 (0.30%)	
occurrences (all)	1	1	
Procedural dizziness			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	

Procedural hypotension			
subjects affected / exposed	1 / 675 (0.15%)	1 / 336 (0.30%)	
occurrences (all)	1	1	
Procedural nausea			
subjects affected / exposed	10 / 675 (1.48%)	5 / 336 (1.49%)	
occurrences (all)	11	5	
Procedural pain			
subjects affected / exposed	43 / 675 (6.37%)	22 / 336 (6.55%)	
occurrences (all)	46	22	
Rib fracture			
subjects affected / exposed	1 / 675 (0.15%)	1 / 336 (0.30%)	
occurrences (all)	1	1	
Seroma			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Skin abrasion			
subjects affected / exposed	3 / 675 (0.44%)	1 / 336 (0.30%)	
occurrences (all)	3	3	
Stoma site haemorrhage			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Stoma site inflammation			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Stoma site irritation			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Stoma site reaction			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Thermal burn			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Tooth fracture			
subjects affected / exposed	1 / 675 (0.15%)	1 / 336 (0.30%)	
occurrences (all)	1	1	

Upper limb fracture			
subjects affected / exposed	4 / 675 (0.59%)	0 / 336 (0.00%)	
occurrences (all)	4	0	
Venous injury			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Wound			
subjects affected / exposed	6 / 675 (0.89%)	2 / 336 (0.60%)	
occurrences (all)	6	2	
Wound complication			
subjects affected / exposed	11 / 675 (1.63%)	7 / 336 (2.08%)	
occurrences (all)	12	7	
Wound decomposition			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	2	0	
Wound dehiscence			
subjects affected / exposed	3 / 675 (0.44%)	0 / 336 (0.00%)	
occurrences (all)	4	0	
Wound evisceration			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Wound haemorrhage			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Wound secretion			
subjects affected / exposed	2 / 675 (0.30%)	3 / 336 (0.89%)	
occurrences (all)	2	3	
Wrist fracture			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Congenital, familial and genetic disorders			
Bronchogenic cyst			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Familial tremor			

subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Arrhythmia			
subjects affected / exposed	1 / 675 (0.15%)	2 / 336 (0.60%)	
occurrences (all)	1	3	
Arrhythmia supraventricular			
subjects affected / exposed	2 / 675 (0.30%)	0 / 336 (0.00%)	
occurrences (all)	2	0	
Atrial fibrillation			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Atrial flutter			
subjects affected / exposed	1 / 675 (0.15%)	1 / 336 (0.30%)	
occurrences (all)	1	1	
Atrial tachycardia			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Atrioventricular block			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	2	
Bradycardia			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Bundle branch block left			
subjects affected / exposed	1 / 675 (0.15%)	1 / 336 (0.30%)	
occurrences (all)	1	1	
Cardiac failure			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Cardiac failure chronic			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	

Cardiac flutter			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Cardiomegaly			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Cardiovascular disorder			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Congestive cardiomyopathy			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Myocardial ischaemia			
subjects affected / exposed	2 / 675 (0.30%)	0 / 336 (0.00%)	
occurrences (all)	3	0	
Nodal arrhythmia			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Palpitations			
subjects affected / exposed	20 / 675 (2.96%)	16 / 336 (4.76%)	
occurrences (all)	23	17	
Pericardial effusion			
subjects affected / exposed	5 / 675 (0.74%)	1 / 336 (0.30%)	
occurrences (all)	5	1	
Sinus bradycardia			
subjects affected / exposed	1 / 675 (0.15%)	1 / 336 (0.30%)	
occurrences (all)	1	1	
Sinus tachycardia			
subjects affected / exposed	7 / 675 (1.04%)	3 / 336 (0.89%)	
occurrences (all)	7	3	
Supraventricular tachycardia			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Tachycardia			
subjects affected / exposed	13 / 675 (1.93%)	10 / 336 (2.98%)	
occurrences (all)	13	11	

Tachycardia foetal			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Ventricular extrasystoles			
subjects affected / exposed	3 / 675 (0.44%)	1 / 336 (0.30%)	
occurrences (all)	3	1	
Ventricular flutter			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Ventricular tachycardia			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			
Amnesia			
subjects affected / exposed	5 / 675 (0.74%)	1 / 336 (0.30%)	
occurrences (all)	5	1	
Anosmia			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Aphasia			
subjects affected / exposed	2 / 675 (0.30%)	1 / 336 (0.30%)	
occurrences (all)	2	1	
Aphonia			
subjects affected / exposed	1 / 675 (0.15%)	1 / 336 (0.30%)	
occurrences (all)	1	1	
Ataxia			
subjects affected / exposed	3 / 675 (0.44%)	0 / 336 (0.00%)	
occurrences (all)	4	0	
Aura			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Balance disorder			
subjects affected / exposed	3 / 675 (0.44%)	4 / 336 (1.19%)	
occurrences (all)	3	5	
Burning sensation			

subjects affected / exposed	2 / 675 (0.30%)	2 / 336 (0.60%)	
occurrences (all)	2	3	
Carpal tunnel syndrome			
subjects affected / exposed	2 / 675 (0.30%)	1 / 336 (0.30%)	
occurrences (all)	2	1	
Cognitive disorder			
subjects affected / exposed	0 / 675 (0.00%)	4 / 336 (1.19%)	
occurrences (all)	0	4	
Cranial nerve disorder			
subjects affected / exposed	1 / 675 (0.15%)	1 / 336 (0.30%)	
occurrences (all)	1	2	
Depressed level of consciousness			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	2	0	
Diabetic neuropathy			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	2	0	
Disturbance in attention			
subjects affected / exposed	2 / 675 (0.30%)	0 / 336 (0.00%)	
occurrences (all)	2	0	
Dizziness			
subjects affected / exposed	128 / 675 (18.96%)	48 / 336 (14.29%)	
occurrences (all)	211	68	
Dizziness exertional			
subjects affected / exposed	2 / 675 (0.30%)	0 / 336 (0.00%)	
occurrences (all)	2	0	
Dizziness postural			
subjects affected / exposed	7 / 675 (1.04%)	1 / 336 (0.30%)	
occurrences (all)	10	1	
Dysaesthesia			
subjects affected / exposed	3 / 675 (0.44%)	3 / 336 (0.89%)	
occurrences (all)	5	4	
Dysarthria			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Dysgeusia			

subjects affected / exposed	71 / 675 (10.52%)	37 / 336 (11.01%)	
occurrences (all)	84	50	
Dyskinesia			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Facial paralysis			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Head discomfort			
subjects affected / exposed	1 / 675 (0.15%)	1 / 336 (0.30%)	
occurrences (all)	1	1	
Headache			
subjects affected / exposed	121 / 675 (17.93%)	51 / 336 (15.18%)	
occurrences (all)	182	90	
Horner's syndrome			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	3	0	
Hyperaesthesia			
subjects affected / exposed	1 / 675 (0.15%)	1 / 336 (0.30%)	
occurrences (all)	1	1	
Hypoaesthesia			
subjects affected / exposed	24 / 675 (3.56%)	10 / 336 (2.98%)	
occurrences (all)	33	12	
Lethargy			
subjects affected / exposed	4 / 675 (0.59%)	1 / 336 (0.30%)	
occurrences (all)	4	1	
Memory impairment			
subjects affected / exposed	7 / 675 (1.04%)	6 / 336 (1.79%)	
occurrences (all)	7	6	
Mental impairment			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Meralgia paraesthetica			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Migraine			

subjects affected / exposed	4 / 675 (0.59%)	1 / 336 (0.30%)	
occurrences (all)	5	1	
Migraine with aura			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Motor dysfunction			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Myoclonus			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Nervous system disorder			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Neuralgia			
subjects affected / exposed	5 / 675 (0.74%)	0 / 336 (0.00%)	
occurrences (all)	11	0	
Neuropathy peripheral			
subjects affected / exposed	215 / 675 (31.85%)	103 / 336 (30.65%)	
occurrences (all)	363	173	
Neurotoxicity			
subjects affected / exposed	19 / 675 (2.81%)	12 / 336 (3.57%)	
occurrences (all)	30	23	
Olfactory nerve disorder			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Paraesthesia			
subjects affected / exposed	74 / 675 (10.96%)	41 / 336 (12.20%)	
occurrences (all)	101	66	
Parosmia			
subjects affected / exposed	1 / 675 (0.15%)	1 / 336 (0.30%)	
occurrences (all)	1	1	
Peripheral motor neuropathy			
subjects affected / exposed	7 / 675 (1.04%)	2 / 336 (0.60%)	
occurrences (all)	8	2	
Peripheral sensorimotor neuropathy			

subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	6	0	
Peripheral sensory neuropathy			
subjects affected / exposed	139 / 675 (20.59%)	65 / 336 (19.35%)	
occurrences (all)	208	111	
Peroneal nerve palsy			
subjects affected / exposed	1 / 675 (0.15%)	1 / 336 (0.30%)	
occurrences (all)	1	1	
Polyneuropathy			
subjects affected / exposed	22 / 675 (3.26%)	16 / 336 (4.76%)	
occurrences (all)	28	27	
Poor quality sleep			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Post herpetic neuralgia			
subjects affected / exposed	2 / 675 (0.30%)	1 / 336 (0.30%)	
occurrences (all)	2	1	
Post-traumatic headache			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Presyncope			
subjects affected / exposed	2 / 675 (0.30%)	1 / 336 (0.30%)	
occurrences (all)	2	1	
Radicular pain			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Restless legs syndrome			
subjects affected / exposed	13 / 675 (1.93%)	9 / 336 (2.68%)	
occurrences (all)	15	10	
Reversed hot-cold sensation			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Sciatica			
subjects affected / exposed	5 / 675 (0.74%)	4 / 336 (1.19%)	
occurrences (all)	11	5	
Seizure			

subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Sensory disturbance			
subjects affected / exposed	1 / 675 (0.15%)	2 / 336 (0.60%)	
occurrences (all)	2	2	
Sinus headache			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Somnolence			
subjects affected / exposed	8 / 675 (1.19%)	5 / 336 (1.49%)	
occurrences (all)	8	6	
Speech disorder			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Syncope			
subjects affected / exposed	18 / 675 (2.67%)	10 / 336 (2.98%)	
occurrences (all)	22	10	
Tension headache			
subjects affected / exposed	2 / 675 (0.30%)	0 / 336 (0.00%)	
occurrences (all)	2	0	
Thoracic outlet syndrome			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Toxic neuropathy			
subjects affected / exposed	0 / 675 (0.00%)	2 / 336 (0.60%)	
occurrences (all)	0	3	
Tremor			
subjects affected / exposed	11 / 675 (1.63%)	5 / 336 (1.49%)	
occurrences (all)	12	7	
Trigeminal neuralgia			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	201 / 675 (29.78%)	112 / 336 (33.33%)	
occurrences (all)	556	306	

Anaemia vitamin b12 deficiency			
subjects affected / exposed	1 / 675 (0.15%)	1 / 336 (0.30%)	
occurrences (all)	1	1	
Coagulopathy			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Febrile neutropenia			
subjects affected / exposed	5 / 675 (0.74%)	2 / 336 (0.60%)	
occurrences (all)	5	2	
Haematotoxicity			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Hypercoagulation			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Hypochromasia			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Increased tendency to bruise			
subjects affected / exposed	2 / 675 (0.30%)	1 / 336 (0.30%)	
occurrences (all)	2	1	
Iron deficiency anaemia			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	2	0	
Leukocytosis			
subjects affected / exposed	0 / 675 (0.00%)	2 / 336 (0.60%)	
occurrences (all)	0	2	
Leukopenia			
subjects affected / exposed	116 / 675 (17.19%)	58 / 336 (17.26%)	
occurrences (all)	466	205	
Lymph node pain			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Lymphadenitis			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	

Lymphadenopathy			
subjects affected / exposed	1 / 675 (0.15%)	1 / 336 (0.30%)	
occurrences (all)	1	1	
Lymphopenia			
subjects affected / exposed	9 / 675 (1.33%)	4 / 336 (1.19%)	
occurrences (all)	43	12	
Neutropenia			
subjects affected / exposed	296 / 675 (43.85%)	157 / 336 (46.73%)	
occurrences (all)	1104	532	
Normochromic normocytic anaemia			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Pancytopenia			
subjects affected / exposed	1 / 675 (0.15%)	3 / 336 (0.89%)	
occurrences (all)	4	7	
Platelet disorder			
subjects affected / exposed	6 / 675 (0.89%)	3 / 336 (0.89%)	
occurrences (all)	6	8	
Thrombasthenia			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Thrombocytopenia			
subjects affected / exposed	131 / 675 (19.41%)	59 / 336 (17.56%)	
occurrences (all)	340	160	
Thrombocytosis			
subjects affected / exposed	2 / 675 (0.30%)	1 / 336 (0.30%)	
occurrences (all)	2	1	
White blood cell disorder			
subjects affected / exposed	3 / 675 (0.44%)	2 / 336 (0.60%)	
occurrences (all)	12	2	
Ear and labyrinth disorders			
Cerumen impaction			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Conductive deafness			

subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Deafness			
subjects affected / exposed	6 / 675 (0.89%)	2 / 336 (0.60%)	
occurrences (all)	6	4	
Deafness bilateral			
subjects affected / exposed	1 / 675 (0.15%)	1 / 336 (0.30%)	
occurrences (all)	1	1	
Deafness unilateral			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Ear congestion			
subjects affected / exposed	1 / 675 (0.15%)	1 / 336 (0.30%)	
occurrences (all)	1	1	
Ear discomfort			
subjects affected / exposed	1 / 675 (0.15%)	1 / 336 (0.30%)	
occurrences (all)	1	1	
Ear disorder			
subjects affected / exposed	2 / 675 (0.30%)	0 / 336 (0.00%)	
occurrences (all)	2	0	
Ear pain			
subjects affected / exposed	13 / 675 (1.93%)	6 / 336 (1.79%)	
occurrences (all)	17	7	
Eustachian tube dysfunction			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Eustachian tube patulous			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Hypoacusis			
subjects affected / exposed	4 / 675 (0.59%)	1 / 336 (0.30%)	
occurrences (all)	4	1	
Motion sickness			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Ototoxicity			

subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Tinnitus			
subjects affected / exposed	26 / 675 (3.85%)	6 / 336 (1.79%)	
occurrences (all)	28	9	
Vertigo			
subjects affected / exposed	21 / 675 (3.11%)	4 / 336 (1.19%)	
occurrences (all)	25	8	
Vertigo positional			
subjects affected / exposed	1 / 675 (0.15%)	1 / 336 (0.30%)	
occurrences (all)	1	1	
Eye disorders			
Age-related macular degeneration			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Amblyopia			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Asthenopia			
subjects affected / exposed	0 / 675 (0.00%)	3 / 336 (0.89%)	
occurrences (all)	0	3	
Blepharospasm			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Cataract			
subjects affected / exposed	5 / 675 (0.74%)	2 / 336 (0.60%)	
occurrences (all)	6	2	
Chalazion			
subjects affected / exposed	1 / 675 (0.15%)	2 / 336 (0.60%)	
occurrences (all)	1	2	
Conjunctival haemorrhage			
subjects affected / exposed	1 / 675 (0.15%)	2 / 336 (0.60%)	
occurrences (all)	1	3	
Conjunctival oedema			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	2	0	

Dacryostenosis acquired			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Diplopia			
subjects affected / exposed	5 / 675 (0.74%)	0 / 336 (0.00%)	
occurrences (all)	5	0	
Dry eye			
subjects affected / exposed	24 / 675 (3.56%)	9 / 336 (2.68%)	
occurrences (all)	30	9	
Eye allergy			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Eye discharge			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Eye disorder			
subjects affected / exposed	4 / 675 (0.59%)	2 / 336 (0.60%)	
occurrences (all)	4	2	
Eye haemorrhage			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Eye irritation			
subjects affected / exposed	1 / 675 (0.15%)	3 / 336 (0.89%)	
occurrences (all)	1	4	
Eye movement disorder			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	2	
Eye pain			
subjects affected / exposed	3 / 675 (0.44%)	0 / 336 (0.00%)	
occurrences (all)	4	0	
Eye pruritus			
subjects affected / exposed	5 / 675 (0.74%)	0 / 336 (0.00%)	
occurrences (all)	5	0	
Eyelid irritation			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	

Eyelid ptosis			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Foreign body sensation in eyes			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Glaucoma			
subjects affected / exposed	5 / 675 (0.74%)	0 / 336 (0.00%)	
occurrences (all)	5	0	
Hypermetropia			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Lacrimation increased			
subjects affected / exposed	19 / 675 (2.81%)	2 / 336 (0.60%)	
occurrences (all)	21	2	
Maculopathy			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Ocular discomfort			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Ocular hyperaemia			
subjects affected / exposed	0 / 675 (0.00%)	2 / 336 (0.60%)	
occurrences (all)	0	2	
Ocular hypertension			
subjects affected / exposed	3 / 675 (0.44%)	0 / 336 (0.00%)	
occurrences (all)	3	0	
Photophobia			
subjects affected / exposed	1 / 675 (0.15%)	1 / 336 (0.30%)	
occurrences (all)	1	1	
Photopsia			
subjects affected / exposed	2 / 675 (0.30%)	1 / 336 (0.30%)	
occurrences (all)	2	1	
Presbyopia			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	

Pterygium			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Punctate keratitis			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Retinal vein occlusion			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Scleral cyst			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Scleral disorder			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Scleral haemorrhage			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Vision blurred			
subjects affected / exposed	74 / 675 (10.96%)	24 / 336 (7.14%)	
occurrences (all)	85	30	
Visual acuity reduced			
subjects affected / exposed	7 / 675 (1.04%)	1 / 336 (0.30%)	
occurrences (all)	8	1	
Vitreous detachment			
subjects affected / exposed	3 / 675 (0.44%)	1 / 336 (0.30%)	
occurrences (all)	3	1	
Visual impairment			
subjects affected / exposed	7 / 675 (1.04%)	4 / 336 (1.19%)	
occurrences (all)	9	4	
Vitreous haemorrhage			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Vitreous floaters			
subjects affected / exposed	4 / 675 (0.59%)	1 / 336 (0.30%)	
occurrences (all)	4	1	

Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	18 / 675 (2.67%)	11 / 336 (3.27%)	
occurrences (all)	20	11	
Abdominal distension			
subjects affected / exposed	71 / 675 (10.52%)	25 / 336 (7.44%)	
occurrences (all)	95	27	
Abdominal hernia			
subjects affected / exposed	3 / 675 (0.44%)	0 / 336 (0.00%)	
occurrences (all)	3	0	
Abdominal pain			
subjects affected / exposed	212 / 675 (31.41%)	109 / 336 (32.44%)	
occurrences (all)	372	179	
Abdominal pain lower			
subjects affected / exposed	26 / 675 (3.85%)	10 / 336 (2.98%)	
occurrences (all)	31	11	
Abdominal pain upper			
subjects affected / exposed	72 / 675 (10.67%)	35 / 336 (10.42%)	
occurrences (all)	102	47	
Abdominal rigidity			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Abdominal tenderness			
subjects affected / exposed	1 / 675 (0.15%)	1 / 336 (0.30%)	
occurrences (all)	1	1	
Anal fissure			
subjects affected / exposed	1 / 675 (0.15%)	1 / 336 (0.30%)	
occurrences (all)	1	1	
Anal incontinence			
subjects affected / exposed	1 / 675 (0.15%)	1 / 336 (0.30%)	
occurrences (all)	1	1	
Anal haemorrhage			
subjects affected / exposed	1 / 675 (0.15%)	1 / 336 (0.30%)	
occurrences (all)	1	1	
Anal pruritus			

subjects affected / exposed	2 / 675 (0.30%)	0 / 336 (0.00%)	
occurrences (all)	2	0	
Anal sphincter atony			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Anal ulcer			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Anorectal discomfort			
subjects affected / exposed	2 / 675 (0.30%)	0 / 336 (0.00%)	
occurrences (all)	2	0	
Aphthous ulcer			
subjects affected / exposed	6 / 675 (0.89%)	2 / 336 (0.60%)	
occurrences (all)	7	6	
Ascites			
subjects affected / exposed	91 / 675 (13.48%)	21 / 336 (6.25%)	
occurrences (all)	172	29	
Bowel movement irregularity			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Change of bowel habit			
subjects affected / exposed	2 / 675 (0.30%)	1 / 336 (0.30%)	
occurrences (all)	2	1	
Chapped lips			
subjects affected / exposed	0 / 675 (0.00%)	2 / 336 (0.60%)	
occurrences (all)	0	2	
Colitis			
subjects affected / exposed	1 / 675 (0.15%)	1 / 336 (0.30%)	
occurrences (all)	1	1	
Cheilitis			
subjects affected / exposed	1 / 675 (0.15%)	2 / 336 (0.60%)	
occurrences (all)	1	2	
Constipation			
subjects affected / exposed	267 / 675 (39.56%)	143 / 336 (42.56%)	
occurrences (all)	397	207	
Defaecation urgency			

subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Dental caries			
subjects affected / exposed	3 / 675 (0.44%)	5 / 336 (1.49%)	
occurrences (all)	3	5	
Diarrhoea			
subjects affected / exposed	238 / 675 (35.26%)	116 / 336 (34.52%)	
occurrences (all)	423	203	
Diarrhoea haemorrhagic			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Douglas' pouch mass			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Dry mouth			
subjects affected / exposed	24 / 675 (3.56%)	11 / 336 (3.27%)	
occurrences (all)	27	12	
Dyschezia			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Dyspepsia			
subjects affected / exposed	78 / 675 (11.56%)	33 / 336 (9.82%)	
occurrences (all)	96	38	
Dysphagia			
subjects affected / exposed	2 / 675 (0.30%)	1 / 336 (0.30%)	
occurrences (all)	2	1	
Enteritis			
subjects affected / exposed	3 / 675 (0.44%)	2 / 336 (0.60%)	
occurrences (all)	4	2	
Enterocolitis			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Epigastric discomfort			
subjects affected / exposed	7 / 675 (1.04%)	5 / 336 (1.49%)	
occurrences (all)	9	5	
Eructation			

subjects affected / exposed	4 / 675 (0.59%)	2 / 336 (0.60%)	
occurrences (all)	4	2	
Faecaloma			
subjects affected / exposed	1 / 675 (0.15%)	1 / 336 (0.30%)	
occurrences (all)	1	1	
Faeces soft			
subjects affected / exposed	1 / 675 (0.15%)	2 / 336 (0.60%)	
occurrences (all)	1	3	
Flatulence			
subjects affected / exposed	26 / 675 (3.85%)	9 / 336 (2.68%)	
occurrences (all)	30	10	
Food poisoning			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Frequent bowel movements			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	2	0	
Functional gastrointestinal disorder			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Gastric disorder			
subjects affected / exposed	1 / 675 (0.15%)	1 / 336 (0.30%)	
occurrences (all)	1	1	
Gastric ulcer			
subjects affected / exposed	1 / 675 (0.15%)	2 / 336 (0.60%)	
occurrences (all)	1	2	
Gastritis			
subjects affected / exposed	7 / 675 (1.04%)	5 / 336 (1.49%)	
occurrences (all)	8	5	
Gastritis erosive			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal haemorrhage			
subjects affected / exposed	1 / 675 (0.15%)	1 / 336 (0.30%)	
occurrences (all)	1	1	
Gastrointestinal disorder			

subjects affected / exposed	2 / 675 (0.30%)	2 / 336 (0.60%)	
occurrences (all)	2	2	
Gastrointestinal motility disorder			
subjects affected / exposed	2 / 675 (0.30%)	3 / 336 (0.89%)	
occurrences (all)	2	3	
Gastrointestinal obstruction			
subjects affected / exposed	2 / 675 (0.30%)	1 / 336 (0.30%)	
occurrences (all)	2	1	
Gastrointestinal pain			
subjects affected / exposed	6 / 675 (0.89%)	0 / 336 (0.00%)	
occurrences (all)	6	0	
Gastrointestinal sounds abnormal			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Gastrooesophageal reflux disease			
subjects affected / exposed	22 / 675 (3.26%)	9 / 336 (2.68%)	
occurrences (all)	24	10	
Gingival bleeding			
subjects affected / exposed	1 / 675 (0.15%)	3 / 336 (0.89%)	
occurrences (all)	1	4	
Gingival pain			
subjects affected / exposed	6 / 675 (0.89%)	1 / 336 (0.30%)	
occurrences (all)	6	1	
Gingival swelling			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Haematochezia			
subjects affected / exposed	5 / 675 (0.74%)	3 / 336 (0.89%)	
occurrences (all)	5	3	
Haemorrhoidal haemorrhage			
subjects affected / exposed	0 / 675 (0.00%)	2 / 336 (0.60%)	
occurrences (all)	0	2	
Haemorrhoids			
subjects affected / exposed	19 / 675 (2.81%)	5 / 336 (1.49%)	
occurrences (all)	23	5	
Hiatus hernia			

subjects affected / exposed	2 / 675 (0.30%)	0 / 336 (0.00%)	
occurrences (all)	2	0	
Hyperchlorhydria			
subjects affected / exposed	1 / 675 (0.15%)	1 / 336 (0.30%)	
occurrences (all)	1	1	
Hypoaesthesia oral			
subjects affected / exposed	1 / 675 (0.15%)	2 / 336 (0.60%)	
occurrences (all)	1	2	
Ileus			
subjects affected / exposed	8 / 675 (1.19%)	2 / 336 (0.60%)	
occurrences (all)	9	3	
Inguinal hernia			
subjects affected / exposed	1 / 675 (0.15%)	1 / 336 (0.30%)	
occurrences (all)	1	1	
Intestinal fistula			
subjects affected / exposed	1 / 675 (0.15%)	1 / 336 (0.30%)	
occurrences (all)	1	1	
Intestinal obstruction			
subjects affected / exposed	3 / 675 (0.44%)	0 / 336 (0.00%)	
occurrences (all)	5	0	
Intra-abdominal haemorrhage			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Large intestinal obstruction			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Large intestine perforation			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Large intestine polyp			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Lip blister			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Lip pain			

subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Lip ulceration			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	2	0	
Melaena			
subjects affected / exposed	1 / 675 (0.15%)	1 / 336 (0.30%)	
occurrences (all)	1	1	
Mouth haemorrhage			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Mouth ulceration			
subjects affected / exposed	4 / 675 (0.59%)	0 / 336 (0.00%)	
occurrences (all)	5	0	
Nausea			
subjects affected / exposed	387 / 675 (57.33%)	205 / 336 (61.01%)	
occurrences (all)	835	375	
Odynophagia			
subjects affected / exposed	4 / 675 (0.59%)	2 / 336 (0.60%)	
occurrences (all)	4	6	
Oesophageal pain			
subjects affected / exposed	1 / 675 (0.15%)	1 / 336 (0.30%)	
occurrences (all)	1	1	
Oesophageal spasm			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Oesophagitis			
subjects affected / exposed	4 / 675 (0.59%)	3 / 336 (0.89%)	
occurrences (all)	4	3	
Oral disorder			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Oral mucosal erythema			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Oral mucosal exfoliation			

subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Oral pain			
subjects affected / exposed	4 / 675 (0.59%)	6 / 336 (1.79%)	
occurrences (all)	4	7	
Pancreatitis chronic			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Parotid duct obstruction			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Perianal erythema			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Periodontal disease			
subjects affected / exposed	2 / 675 (0.30%)	0 / 336 (0.00%)	
occurrences (all)	2	0	
Proctalgia			
subjects affected / exposed	4 / 675 (0.59%)	3 / 336 (0.89%)	
occurrences (all)	4	3	
Rectal discharge			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Rectal fissure			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Rectal haemorrhage			
subjects affected / exposed	6 / 675 (0.89%)	4 / 336 (1.19%)	
occurrences (all)	8	5	
Retching			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Salivary gland pain			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Salivary hypersecretion			

subjects affected / exposed	2 / 675 (0.30%)	0 / 336 (0.00%)	
occurrences (all)	4	0	
Sensitivity of teeth			
subjects affected / exposed	2 / 675 (0.30%)	1 / 336 (0.30%)	
occurrences (all)	2	2	
Small intestinal obstruction			
subjects affected / exposed	2 / 675 (0.30%)	1 / 336 (0.30%)	
occurrences (all)	2	1	
Stomatitis			
subjects affected / exposed	41 / 675 (6.07%)	21 / 336 (6.25%)	
occurrences (all)	50	21	
Subileus			
subjects affected / exposed	1 / 675 (0.15%)	2 / 336 (0.60%)	
occurrences (all)	2	2	
Tongue coated			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Tongue discolouration			
subjects affected / exposed	3 / 675 (0.44%)	1 / 336 (0.30%)	
occurrences (all)	3	2	
Tooth disorder			
subjects affected / exposed	0 / 675 (0.00%)	2 / 336 (0.60%)	
occurrences (all)	0	2	
Tooth loss			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Toothache			
subjects affected / exposed	22 / 675 (3.26%)	11 / 336 (3.27%)	
occurrences (all)	25	12	
Umbilical hernia			
subjects affected / exposed	1 / 675 (0.15%)	3 / 336 (0.89%)	
occurrences (all)	1	3	
Vomiting			
subjects affected / exposed	233 / 675 (34.52%)	109 / 336 (32.44%)	
occurrences (all)	383	176	
Skin and subcutaneous tissue disorders			

Alopecia			
subjects affected / exposed	363 / 675 (53.78%)	179 / 336 (53.27%)	
occurrences (all)	507	257	
Acne			
subjects affected / exposed	4 / 675 (0.59%)	1 / 336 (0.30%)	
occurrences (all)	7	1	
Alopecia totalis			
subjects affected / exposed	1 / 675 (0.15%)	4 / 336 (1.19%)	
occurrences (all)	1	4	
Alopecia areata			
subjects affected / exposed	2 / 675 (0.30%)	6 / 336 (1.79%)	
occurrences (all)	2	9	
Blister			
subjects affected / exposed	2 / 675 (0.30%)	1 / 336 (0.30%)	
occurrences (all)	2	1	
Dermal cyst			
subjects affected / exposed	2 / 675 (0.30%)	0 / 336 (0.00%)	
occurrences (all)	2	0	
Dermatitis			
subjects affected / exposed	6 / 675 (0.89%)	3 / 336 (0.89%)	
occurrences (all)	6	4	
Dermatitis acneiform			
subjects affected / exposed	9 / 675 (1.33%)	4 / 336 (1.19%)	
occurrences (all)	11	6	
Dermatitis allergic			
subjects affected / exposed	1 / 675 (0.15%)	3 / 336 (0.89%)	
occurrences (all)	1	3	
Dermatitis bullous			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Dermatitis contact			
subjects affected / exposed	2 / 675 (0.30%)	0 / 336 (0.00%)	
occurrences (all)	2	0	
Diabetic foot			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	2	0	

Dry skin			
subjects affected / exposed	24 / 675 (3.56%)	15 / 336 (4.46%)	
occurrences (all)	27	15	
Ecchymosis			
subjects affected / exposed	3 / 675 (0.44%)	1 / 336 (0.30%)	
occurrences (all)	3	1	
Eczema			
subjects affected / exposed	2 / 675 (0.30%)	2 / 336 (0.60%)	
occurrences (all)	2	2	
Erythema			
subjects affected / exposed	24 / 675 (3.56%)	13 / 336 (3.87%)	
occurrences (all)	33	15	
Erythema multiforme			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Exfoliative rash			
subjects affected / exposed	7 / 675 (1.04%)	0 / 336 (0.00%)	
occurrences (all)	9	0	
Excessive granulation tissue			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Hair growth abnormal			
subjects affected / exposed	5 / 675 (0.74%)	3 / 336 (0.89%)	
occurrences (all)	6	3	
Hidradenitis			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Hyperhidrosis			
subjects affected / exposed	7 / 675 (1.04%)	8 / 336 (2.38%)	
occurrences (all)	8	9	
Hirsutism			
subjects affected / exposed	2 / 675 (0.30%)	0 / 336 (0.00%)	
occurrences (all)	2	0	
Hyperkeratosis			
subjects affected / exposed	4 / 675 (0.59%)	0 / 336 (0.00%)	
occurrences (all)	5	0	

Ingrowing nail			
subjects affected / exposed	2 / 675 (0.30%)	1 / 336 (0.30%)	
occurrences (all)	2	1	
Lichen sclerosus			
subjects affected / exposed	1 / 675 (0.15%)	1 / 336 (0.30%)	
occurrences (all)	1	1	
Madarosis			
subjects affected / exposed	3 / 675 (0.44%)	1 / 336 (0.30%)	
occurrences (all)	3	1	
Nail bed inflammation			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Nail discolouration			
subjects affected / exposed	3 / 675 (0.44%)	3 / 336 (0.89%)	
occurrences (all)	3	3	
Nail disorder			
subjects affected / exposed	17 / 675 (2.52%)	7 / 336 (2.08%)	
occurrences (all)	21	7	
Nail dystrophy			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Neurodermatitis			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Night sweats			
subjects affected / exposed	11 / 675 (1.63%)	3 / 336 (0.89%)	
occurrences (all)	12	3	
Onychoclasis			
subjects affected / exposed	1 / 675 (0.15%)	6 / 336 (1.79%)	
occurrences (all)	1	6	
Onychomadesis			
subjects affected / exposed	2 / 675 (0.30%)	1 / 336 (0.30%)	
occurrences (all)	2	1	
Pain of skin			
subjects affected / exposed	2 / 675 (0.30%)	3 / 336 (0.89%)	
occurrences (all)	2	3	

Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	5 / 675 (0.74%)	2 / 336 (0.60%)	
occurrences (all)	5	2	
Panniculitis			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Papule			
subjects affected / exposed	2 / 675 (0.30%)	0 / 336 (0.00%)	
occurrences (all)	2	0	
Petechiae			
subjects affected / exposed	4 / 675 (0.59%)	4 / 336 (1.19%)	
occurrences (all)	4	4	
Photosensitivity reaction			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Pigmentation disorder			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Piloerection			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Pityriasis			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Pruritus			
subjects affected / exposed	69 / 675 (10.22%)	29 / 336 (8.63%)	
occurrences (all)	84	41	
Pruritus allergic			
subjects affected / exposed	1 / 675 (0.15%)	1 / 336 (0.30%)	
occurrences (all)	1	1	
Pruritus generalised			
subjects affected / exposed	4 / 675 (0.59%)	4 / 336 (1.19%)	
occurrences (all)	4	4	
Psoriasis			

subjects affected / exposed	5 / 675 (0.74%)	0 / 336 (0.00%)	
occurrences (all)	6	0	
Purpura			
subjects affected / exposed	1 / 675 (0.15%)	1 / 336 (0.30%)	
occurrences (all)	1	2	
Rash			
subjects affected / exposed	77 / 675 (11.41%)	49 / 336 (14.58%)	
occurrences (all)	101	66	
Rash erythematous			
subjects affected / exposed	3 / 675 (0.44%)	2 / 336 (0.60%)	
occurrences (all)	4	4	
Rash generalised			
subjects affected / exposed	0 / 675 (0.00%)	4 / 336 (1.19%)	
occurrences (all)	0	4	
Rash macular			
subjects affected / exposed	2 / 675 (0.30%)	1 / 336 (0.30%)	
occurrences (all)	3	1	
Rash maculo-papular			
subjects affected / exposed	3 / 675 (0.44%)	1 / 336 (0.30%)	
occurrences (all)	4	2	
Rash papular			
subjects affected / exposed	1 / 675 (0.15%)	3 / 336 (0.89%)	
occurrences (all)	1	5	
Rash pruritic			
subjects affected / exposed	12 / 675 (1.78%)	5 / 336 (1.49%)	
occurrences (all)	15	5	
Rash vesicular			
subjects affected / exposed	2 / 675 (0.30%)	0 / 336 (0.00%)	
occurrences (all)	2	0	
Rosacea			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Scab			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Scar pain			

subjects affected / exposed	3 / 675 (0.44%)	1 / 336 (0.30%)	
occurrences (all)	3	1	
Seborrhoeic dermatitis			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Skin atrophy			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Skin depigmentation			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Skin discolouration			
subjects affected / exposed	4 / 675 (0.59%)	1 / 336 (0.30%)	
occurrences (all)	5	1	
Skin disorder			
subjects affected / exposed	4 / 675 (0.59%)	1 / 336 (0.30%)	
occurrences (all)	5	1	
Skin exfoliation			
subjects affected / exposed	4 / 675 (0.59%)	1 / 336 (0.30%)	
occurrences (all)	4	1	
Skin fissures			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	3	0	
Skin hyperpigmentation			
subjects affected / exposed	3 / 675 (0.44%)	3 / 336 (0.89%)	
occurrences (all)	3	3	
Skin irritation			
subjects affected / exposed	0 / 675 (0.00%)	3 / 336 (0.89%)	
occurrences (all)	0	4	
Skin lesion			
subjects affected / exposed	3 / 675 (0.44%)	3 / 336 (0.89%)	
occurrences (all)	3	3	
Skin mass			
subjects affected / exposed	3 / 675 (0.44%)	0 / 336 (0.00%)	
occurrences (all)	4	0	
Skin reaction			

subjects affected / exposed	2 / 675 (0.30%)	0 / 336 (0.00%)	
occurrences (all)	2	0	
Skin tightness			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Skin toxicity			
subjects affected / exposed	1 / 675 (0.15%)	1 / 336 (0.30%)	
occurrences (all)	1	1	
Skin ulcer			
subjects affected / exposed	4 / 675 (0.59%)	0 / 336 (0.00%)	
occurrences (all)	8	0	
Stasis dermatitis			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Sweat gland disorder			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Swelling face			
subjects affected / exposed	2 / 675 (0.30%)	0 / 336 (0.00%)	
occurrences (all)	2	0	
Telangiectasia			
subjects affected / exposed	2 / 675 (0.30%)	1 / 336 (0.30%)	
occurrences (all)	2	2	
Toxic skin eruption			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Umbilical discharge			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Urticaria			
subjects affected / exposed	18 / 675 (2.67%)	12 / 336 (3.57%)	
occurrences (all)	21	14	
Urticaria aquagenic			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Xeroderma			

subjects affected / exposed	2 / 675 (0.30%)	0 / 336 (0.00%)	
occurrences (all)	2	0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	3 / 675 (0.44%)	1 / 336 (0.30%)	
occurrences (all)	3	1	
Albuminuria			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Bladder pain			
subjects affected / exposed	2 / 675 (0.30%)	1 / 336 (0.30%)	
occurrences (all)	2	1	
Bladder prolapse			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Bladder spasm			
subjects affected / exposed	1 / 675 (0.15%)	1 / 336 (0.30%)	
occurrences (all)	1	1	
Calculus urinary			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Chronic kidney disease			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Cystitis haemorrhagic			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Cystitis noninfective			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Cystitis-like symptom			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Dysuria			
subjects affected / exposed	29 / 675 (4.30%)	15 / 336 (4.46%)	
occurrences (all)	37	18	

Glycosuria			
subjects affected / exposed	2 / 675 (0.30%)	0 / 336 (0.00%)	
occurrences (all)	2	0	
Haematuria			
subjects affected / exposed	6 / 675 (0.89%)	2 / 336 (0.60%)	
occurrences (all)	6	2	
Hydronephrosis			
subjects affected / exposed	7 / 675 (1.04%)	0 / 336 (0.00%)	
occurrences (all)	7	0	
Incontinence			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Micturition disorder			
subjects affected / exposed	2 / 675 (0.30%)	0 / 336 (0.00%)	
occurrences (all)	2	0	
Micturition urgency			
subjects affected / exposed	7 / 675 (1.04%)	4 / 336 (1.19%)	
occurrences (all)	7	4	
Nephrolithiasis			
subjects affected / exposed	1 / 675 (0.15%)	2 / 336 (0.60%)	
occurrences (all)	1	3	
Neurogenic bladder			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Nocturia			
subjects affected / exposed	3 / 675 (0.44%)	1 / 336 (0.30%)	
occurrences (all)	5	1	
Oliguria			
subjects affected / exposed	5 / 675 (0.74%)	1 / 336 (0.30%)	
occurrences (all)	5	1	
Pollakiuria			
subjects affected / exposed	18 / 675 (2.67%)	10 / 336 (2.98%)	
occurrences (all)	19	10	
Polyuria			
subjects affected / exposed	3 / 675 (0.44%)	0 / 336 (0.00%)	
occurrences (all)	3	0	

Proteinuria			
subjects affected / exposed	21 / 675 (3.11%)	9 / 336 (2.68%)	
occurrences (all)	28	11	
Pyelocaliectasis			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Renal aneurysm			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Renal colic			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Renal failure			
subjects affected / exposed	1 / 675 (0.15%)	2 / 336 (0.60%)	
occurrences (all)	1	2	
Renal impairment			
subjects affected / exposed	1 / 675 (0.15%)	1 / 336 (0.30%)	
occurrences (all)	1	1	
Renal pain			
subjects affected / exposed	2 / 675 (0.30%)	2 / 336 (0.60%)	
occurrences (all)	2	2	
Renal vein thrombosis			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Stress urinary incontinence			
subjects affected / exposed	2 / 675 (0.30%)	2 / 336 (0.60%)	
occurrences (all)	2	2	
Urethral pain			
subjects affected / exposed	1 / 675 (0.15%)	1 / 336 (0.30%)	
occurrences (all)	1	1	
Urge incontinence			
subjects affected / exposed	4 / 675 (0.59%)	0 / 336 (0.00%)	
occurrences (all)	4	0	
Urinary bladder rupture			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	

Urinary incontinence			
subjects affected / exposed	16 / 675 (2.37%)	12 / 336 (3.57%)	
occurrences (all)	20	15	
Urinary retention			
subjects affected / exposed	6 / 675 (0.89%)	0 / 336 (0.00%)	
occurrences (all)	6	0	
Urinary tract disorder			
subjects affected / exposed	3 / 675 (0.44%)	0 / 336 (0.00%)	
occurrences (all)	5	0	
Urinary tract pain			
subjects affected / exposed	2 / 675 (0.30%)	0 / 336 (0.00%)	
occurrences (all)	2	0	
Urine abnormality			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Endocrine disorders			
Cushing's syndrome			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Goitre			
subjects affected / exposed	2 / 675 (0.30%)	0 / 336 (0.00%)	
occurrences (all)	2	0	
Hyperparathyroidism primary			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Hyperthyroidism			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Hypothyroidism			
subjects affected / exposed	4 / 675 (0.59%)	4 / 336 (1.19%)	
occurrences (all)	4	4	
Thyroid cyst			
subjects affected / exposed	2 / 675 (0.30%)	0 / 336 (0.00%)	
occurrences (all)	2	0	
Thyroid mass			

subjects affected / exposed	2 / 675 (0.30%)	0 / 336 (0.00%)	
occurrences (all)	2	0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	189 / 675 (28.00%)	92 / 336 (27.38%)	
occurrences (all)	380	173	
Arthritis			
subjects affected / exposed	1 / 675 (0.15%)	2 / 336 (0.60%)	
occurrences (all)	1	2	
Back pain			
subjects affected / exposed	90 / 675 (13.33%)	59 / 336 (17.56%)	
occurrences (all)	124	77	
Bone cyst			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Bone loss			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Bone pain			
subjects affected / exposed	51 / 675 (7.56%)	30 / 336 (8.93%)	
occurrences (all)	66	43	
Bursitis			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Coccydynia			
subjects affected / exposed	2 / 675 (0.30%)	0 / 336 (0.00%)	
occurrences (all)	4	0	
Costochondritis			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Exostosis			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Fistula			

subjects affected / exposed	2 / 675 (0.30%)	0 / 336 (0.00%)	
occurrences (all)	2	0	
Flank pain			
subjects affected / exposed	13 / 675 (1.93%)	4 / 336 (1.19%)	
occurrences (all)	15	4	
Fracture pain			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Groin pain			
subjects affected / exposed	12 / 675 (1.78%)	3 / 336 (0.89%)	
occurrences (all)	15	3	
Intervertebral disc degeneration			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Intervertebral disc protrusion			
subjects affected / exposed	1 / 675 (0.15%)	1 / 336 (0.30%)	
occurrences (all)	1	1	
Joint effusion			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Joint stiffness			
subjects affected / exposed	2 / 675 (0.30%)	1 / 336 (0.30%)	
occurrences (all)	3	3	
Joint swelling			
subjects affected / exposed	3 / 675 (0.44%)	0 / 336 (0.00%)	
occurrences (all)	3	0	
Limb discomfort			
subjects affected / exposed	6 / 675 (0.89%)	6 / 336 (1.79%)	
occurrences (all)	7	10	
Muscle contracture			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Muscle fatigue			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Muscle rigidity			

subjects affected / exposed	0 / 675 (0.00%)	2 / 336 (0.60%)	
occurrences (all)	0	2	
Muscle spasms			
subjects affected / exposed	21 / 675 (3.11%)	19 / 336 (5.65%)	
occurrences (all)	24	23	
Muscle tightness			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Muscular weakness			
subjects affected / exposed	33 / 675 (4.89%)	17 / 336 (5.06%)	
occurrences (all)	41	21	
Musculoskeletal chest pain			
subjects affected / exposed	12 / 675 (1.78%)	8 / 336 (2.38%)	
occurrences (all)	13	8	
Musculoskeletal discomfort			
subjects affected / exposed	1 / 675 (0.15%)	1 / 336 (0.30%)	
occurrences (all)	1	1	
Musculoskeletal pain			
subjects affected / exposed	38 / 675 (5.63%)	35 / 336 (10.42%)	
occurrences (all)	47	50	
Musculoskeletal stiffness			
subjects affected / exposed	4 / 675 (0.59%)	3 / 336 (0.89%)	
occurrences (all)	5	5	
Myalgia			
subjects affected / exposed	125 / 675 (18.52%)	64 / 336 (19.05%)	
occurrences (all)	219	117	
Myopathy			
subjects affected / exposed	2 / 675 (0.30%)	1 / 336 (0.30%)	
occurrences (all)	2	1	
Myositis			
subjects affected / exposed	1 / 675 (0.15%)	1 / 336 (0.30%)	
occurrences (all)	3	1	
Neck mass			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Neck pain			

subjects affected / exposed	10 / 675 (1.48%)	7 / 336 (2.08%)	
occurrences (all)	10	8	
Osteoarthritis			
subjects affected / exposed	3 / 675 (0.44%)	4 / 336 (1.19%)	
occurrences (all)	3	4	
Osteomalacia			
subjects affected / exposed	1 / 675 (0.15%)	3 / 336 (0.89%)	
occurrences (all)	2	3	
Osteopenia			
subjects affected / exposed	3 / 675 (0.44%)	0 / 336 (0.00%)	
occurrences (all)	3	0	
Osteoporosis			
subjects affected / exposed	1 / 675 (0.15%)	3 / 336 (0.89%)	
occurrences (all)	1	3	
Pain in extremity			
subjects affected / exposed	118 / 675 (17.48%)	45 / 336 (13.39%)	
occurrences (all)	186	59	
Pain in jaw			
subjects affected / exposed	8 / 675 (1.19%)	5 / 336 (1.49%)	
occurrences (all)	8	5	
Periarthritis			
subjects affected / exposed	2 / 675 (0.30%)	2 / 336 (0.60%)	
occurrences (all)	2	2	
Plantar fasciitis			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	2	0	
Rib deformity			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Sarcopenia			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Sjogren's syndrome			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Soft tissue mass			

subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Soft tissue necrosis			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Spinal osteoarthritis			
subjects affected / exposed	1 / 675 (0.15%)	1 / 336 (0.30%)	
occurrences (all)	1	1	
Spinal pain			
subjects affected / exposed	2 / 675 (0.30%)	3 / 336 (0.89%)	
occurrences (all)	2	3	
Synovial cyst			
subjects affected / exposed	1 / 675 (0.15%)	1 / 336 (0.30%)	
occurrences (all)	1	1	
Temporomandibular joint syndrome			
subjects affected / exposed	1 / 675 (0.15%)	1 / 336 (0.30%)	
occurrences (all)	1	1	
Tendon pain			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Tendonitis			
subjects affected / exposed	4 / 675 (0.59%)	4 / 336 (1.19%)	
occurrences (all)	4	4	
Tenosynovitis			
subjects affected / exposed	1 / 675 (0.15%)	1 / 336 (0.30%)	
occurrences (all)	1	1	
Torticollis			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	2	0	
Infections and infestations			
Abdominal abscess			
subjects affected / exposed	2 / 675 (0.30%)	0 / 336 (0.00%)	
occurrences (all)	3	0	
Abdominal wall infection			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	

Abscess			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Acute sinusitis			
subjects affected / exposed	2 / 675 (0.30%)	2 / 336 (0.60%)	
occurrences (all)	2	2	
Bacteraemia			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Asymptomatic bacteriuria			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Bacterial infection			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	2	0	
Bacterial vaginosis			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Bacteriuria			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Body tinea			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Breast abscess			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Bronchitis			
subjects affected / exposed	10 / 675 (1.48%)	5 / 336 (1.49%)	
occurrences (all)	11	5	
Bronchitis viral			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Catheter site cellulitis			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	

Candida infection			
subjects affected / exposed	3 / 675 (0.44%)	0 / 336 (0.00%)	
occurrences (all)	3	0	
Cellulitis			
subjects affected / exposed	13 / 675 (1.93%)	2 / 336 (0.60%)	
occurrences (all)	14	2	
Catheter site infection			
subjects affected / exposed	3 / 675 (0.44%)	0 / 336 (0.00%)	
occurrences (all)	3	0	
Clostridium difficile colitis			
subjects affected / exposed	2 / 675 (0.30%)	0 / 336 (0.00%)	
occurrences (all)	2	0	
Clostridium colitis			
subjects affected / exposed	1 / 675 (0.15%)	1 / 336 (0.30%)	
occurrences (all)	1	1	
Clostridium difficile infection			
subjects affected / exposed	3 / 675 (0.44%)	0 / 336 (0.00%)	
occurrences (all)	3	0	
Conjunctivitis			
subjects affected / exposed	12 / 675 (1.78%)	6 / 336 (1.79%)	
occurrences (all)	13	6	
Cystitis			
subjects affected / exposed	21 / 675 (3.11%)	6 / 336 (1.79%)	
occurrences (all)	25	7	
Cystitis bacterial			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Cystitis escherichia			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Device related infection			
subjects affected / exposed	5 / 675 (0.74%)	3 / 336 (0.89%)	
occurrences (all)	6	3	
Diarrhoea infectious			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	

Ear infection			
subjects affected / exposed	1 / 675 (0.15%)	1 / 336 (0.30%)	
occurrences (all)	1	1	
Ear lobe infection			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Empyema			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Enteritis infectious			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Erysipelas			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Erysipeloid			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Escherichia infection			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Escherichia urinary tract infection			
subjects affected / exposed	2 / 675 (0.30%)	0 / 336 (0.00%)	
occurrences (all)	2	0	
Eye infection			
subjects affected / exposed	3 / 675 (0.44%)	1 / 336 (0.30%)	
occurrences (all)	4	1	
Folliculitis			
subjects affected / exposed	2 / 675 (0.30%)	2 / 336 (0.60%)	
occurrences (all)	2	2	
Fungal infection			
subjects affected / exposed	3 / 675 (0.44%)	2 / 336 (0.60%)	
occurrences (all)	4	2	
Fungal skin infection			
subjects affected / exposed	1 / 675 (0.15%)	2 / 336 (0.60%)	
occurrences (all)	1	2	

Furuncle			
subjects affected / exposed	1 / 675 (0.15%)	1 / 336 (0.30%)	
occurrences (all)	1	2	
Gastroenteritis			
subjects affected / exposed	7 / 675 (1.04%)	5 / 336 (1.49%)	
occurrences (all)	8	5	
Gastroenteritis viral			
subjects affected / exposed	8 / 675 (1.19%)	0 / 336 (0.00%)	
occurrences (all)	8	0	
Gastrointestinal infection			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Gastrointestinal viral infection			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Genital candidiasis			
subjects affected / exposed	2 / 675 (0.30%)	1 / 336 (0.30%)	
occurrences (all)	2	1	
Genital herpes			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Genitourinary tract infection			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Gingivitis			
subjects affected / exposed	3 / 675 (0.44%)	0 / 336 (0.00%)	
occurrences (all)	3	0	
Groin abscess			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Haematoma infection			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Helicobacter gastritis			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	

Helicobacter infection			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Hepatitis c			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Herpes dermatitis			
subjects affected / exposed	1 / 675 (0.15%)	1 / 336 (0.30%)	
occurrences (all)	1	1	
Herpes simplex			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	2	0	
Herpes virus infection			
subjects affected / exposed	3 / 675 (0.44%)	1 / 336 (0.30%)	
occurrences (all)	3	1	
Herpes zoster			
subjects affected / exposed	8 / 675 (1.19%)	2 / 336 (0.60%)	
occurrences (all)	10	2	
Impetigo			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	2	
Hordeolum			
subjects affected / exposed	3 / 675 (0.44%)	0 / 336 (0.00%)	
occurrences (all)	3	0	
Infected lymphocele			
subjects affected / exposed	1 / 675 (0.15%)	1 / 336 (0.30%)	
occurrences (all)	2	1	
Incision site infection			
subjects affected / exposed	4 / 675 (0.59%)	0 / 336 (0.00%)	
occurrences (all)	5	0	
Infection			
subjects affected / exposed	8 / 675 (1.19%)	2 / 336 (0.60%)	
occurrences (all)	8	2	
Infection parasitic			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	

Infectious pleural effusion			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Influenza			
subjects affected / exposed	18 / 675 (2.67%)	11 / 336 (3.27%)	
occurrences (all)	19	12	
Injection site infection			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Kidney infection			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Laryngitis			
subjects affected / exposed	7 / 675 (1.04%)	2 / 336 (0.60%)	
occurrences (all)	8	2	
Lip infection			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Localised infection			
subjects affected / exposed	3 / 675 (0.44%)	1 / 336 (0.30%)	
occurrences (all)	3	2	
Lung infection			
subjects affected / exposed	2 / 675 (0.30%)	0 / 336 (0.00%)	
occurrences (all)	2	0	
Lower respiratory tract infection			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Lymphangitis			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Mastitis			
subjects affected / exposed	2 / 675 (0.30%)	0 / 336 (0.00%)	
occurrences (all)	4	0	
Mucosal infection			
subjects affected / exposed	1 / 675 (0.15%)	1 / 336 (0.30%)	
occurrences (all)	1	1	

Nail infection			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Nasopharyngitis			
subjects affected / exposed	51 / 675 (7.56%)	31 / 336 (9.23%)	
occurrences (all)	78	44	
Onychomycosis			
subjects affected / exposed	2 / 675 (0.30%)	0 / 336 (0.00%)	
occurrences (all)	2	0	
Oral candidiasis			
subjects affected / exposed	3 / 675 (0.44%)	3 / 336 (0.89%)	
occurrences (all)	3	3	
Oral fungal infection			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Osteomyelitis			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Oral herpes			
subjects affected / exposed	10 / 675 (1.48%)	4 / 336 (1.19%)	
occurrences (all)	10	4	
Paronychia			
subjects affected / exposed	3 / 675 (0.44%)	2 / 336 (0.60%)	
occurrences (all)	4	2	
Pelvic abscess			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Parotitis			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Peritonitis			
subjects affected / exposed	2 / 675 (0.30%)	0 / 336 (0.00%)	
occurrences (all)	2	0	
Periodontitis			
subjects affected / exposed	2 / 675 (0.30%)	0 / 336 (0.00%)	
occurrences (all)	2	0	

Pharyngitis			
subjects affected / exposed	4 / 675 (0.59%)	4 / 336 (1.19%)	
occurrences (all)	5	5	
Pharyngitis bacterial			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Pharyngitis streptococcal			
subjects affected / exposed	2 / 675 (0.30%)	0 / 336 (0.00%)	
occurrences (all)	2	0	
Pharyngotonsillitis			
subjects affected / exposed	1 / 675 (0.15%)	1 / 336 (0.30%)	
occurrences (all)	1	1	
Pneumonia			
subjects affected / exposed	9 / 675 (1.33%)	1 / 336 (0.30%)	
occurrences (all)	9	5	
Post procedural cellulitis			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Post procedural infection			
subjects affected / exposed	2 / 675 (0.30%)	1 / 336 (0.30%)	
occurrences (all)	2	1	
Postoperative wound infection			
subjects affected / exposed	4 / 675 (0.59%)	0 / 336 (0.00%)	
occurrences (all)	5	0	
Pulpitis dental			
subjects affected / exposed	2 / 675 (0.30%)	0 / 336 (0.00%)	
occurrences (all)	3	0	
Pyelonephritis			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	2	
Pyelonephritis acute			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Pyuria			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	

Rash pustular			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Respiratory tract infection			
subjects affected / exposed	12 / 675 (1.78%)	1 / 336 (0.30%)	
occurrences (all)	14	1	
Respiratory tract infection viral			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Rhinitis			
subjects affected / exposed	10 / 675 (1.48%)	9 / 336 (2.68%)	
occurrences (all)	14	10	
Sepsis			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Sialoadenitis			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Sinusitis			
subjects affected / exposed	16 / 675 (2.37%)	5 / 336 (1.49%)	
occurrences (all)	18	7	
Skin candida			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	2	
Skin infection			
subjects affected / exposed	4 / 675 (0.59%)	0 / 336 (0.00%)	
occurrences (all)	6	0	
Staphylococcal infection			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Staphylococcal scalded skin syndrome			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Stoma site abscess			

subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Stoma site infection			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Superinfection			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Tonsillitis			
subjects affected / exposed	2 / 675 (0.30%)	1 / 336 (0.30%)	
occurrences (all)	3	1	
Tinea pedis			
subjects affected / exposed	2 / 675 (0.30%)	0 / 336 (0.00%)	
occurrences (all)	2	0	
Tooth abscess			
subjects affected / exposed	10 / 675 (1.48%)	6 / 336 (1.79%)	
occurrences (all)	14	7	
Tooth infection			
subjects affected / exposed	5 / 675 (0.74%)	2 / 336 (0.60%)	
occurrences (all)	5	2	
Upper respiratory tract infection			
subjects affected / exposed	36 / 675 (5.33%)	11 / 336 (3.27%)	
occurrences (all)	42	16	
Tracheitis			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Urinary tract infection bacterial			
subjects affected / exposed	7 / 675 (1.04%)	2 / 336 (0.60%)	
occurrences (all)	8	2	
Urinary tract infection			
subjects affected / exposed	85 / 675 (12.59%)	36 / 336 (10.71%)	
occurrences (all)	135	52	
Urinary tract infection fungal			
subjects affected / exposed	1 / 675 (0.15%)	1 / 336 (0.30%)	
occurrences (all)	1	1	
Urinary tract infection enterococcal			

subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Urosepsis			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Vaginal abscess			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Vaginal infection			
subjects affected / exposed	4 / 675 (0.59%)	2 / 336 (0.60%)	
occurrences (all)	4	2	
Vaginitis bacterial			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Viral infection			
subjects affected / exposed	3 / 675 (0.44%)	0 / 336 (0.00%)	
occurrences (all)	3	0	
Viral diarrhoea			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Vulvovaginal candidiasis			
subjects affected / exposed	1 / 675 (0.15%)	1 / 336 (0.30%)	
occurrences (all)	1	1	
Vulvovaginal mycotic infection			
subjects affected / exposed	1 / 675 (0.15%)	1 / 336 (0.30%)	
occurrences (all)	1	1	
Wound abscess			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	2	0	
Wound infection			
subjects affected / exposed	5 / 675 (0.74%)	0 / 336 (0.00%)	
occurrences (all)	6	0	
Wound infection staphylococcal			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Metabolism and nutrition disorders			

Abnormal loss of weight			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Decreased appetite			
subjects affected / exposed	175 / 675 (25.93%)	89 / 336 (26.49%)	
occurrences (all)	278	143	
Dehydration			
subjects affected / exposed	34 / 675 (5.04%)	13 / 336 (3.87%)	
occurrences (all)	52	14	
Diabetes mellitus			
subjects affected / exposed	2 / 675 (0.30%)	1 / 336 (0.30%)	
occurrences (all)	2	1	
Fluid imbalance			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Fluid retention			
subjects affected / exposed	3 / 675 (0.44%)	0 / 336 (0.00%)	
occurrences (all)	3	0	
Food craving			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Gout			
subjects affected / exposed	1 / 675 (0.15%)	1 / 336 (0.30%)	
occurrences (all)	2	1	
Hyper hdl cholesterolaemia			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Hypercalcaemia			
subjects affected / exposed	4 / 675 (0.59%)	1 / 336 (0.30%)	
occurrences (all)	4	1	
Hypercholesterolaemia			
subjects affected / exposed	8 / 675 (1.19%)	1 / 336 (0.30%)	
occurrences (all)	8	1	
Hyperglycaemia			
subjects affected / exposed	30 / 675 (4.44%)	12 / 336 (3.57%)	
occurrences (all)	57	31	

Hyperkalaemia			
subjects affected / exposed	11 / 675 (1.63%)	8 / 336 (2.38%)	
occurrences (all)	33	8	
Hyperlipidaemia			
subjects affected / exposed	2 / 675 (0.30%)	0 / 336 (0.00%)	
occurrences (all)	2	0	
Hypernatraemia			
subjects affected / exposed	4 / 675 (0.59%)	0 / 336 (0.00%)	
occurrences (all)	7	0	
Hypertriglyceridaemia			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Hyperuricaemia			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	2	0	
Hypoalbuminaemia			
subjects affected / exposed	40 / 675 (5.93%)	9 / 336 (2.68%)	
occurrences (all)	75	13	
Hypocalcaemia			
subjects affected / exposed	24 / 675 (3.56%)	9 / 336 (2.68%)	
occurrences (all)	43	12	
Hypochloraemia			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Hypoglycaemia			
subjects affected / exposed	3 / 675 (0.44%)	1 / 336 (0.30%)	
occurrences (all)	3	1	
Hypokalaemia			
subjects affected / exposed	115 / 675 (17.04%)	46 / 336 (13.69%)	
occurrences (all)	220	70	
Hypomagnesaemia			
subjects affected / exposed	89 / 675 (13.19%)	41 / 336 (12.20%)	
occurrences (all)	168	79	
Hypometabolism			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	

Hyponatraemia			
subjects affected / exposed	21 / 675 (3.11%)	12 / 336 (3.57%)	
occurrences (all)	32	19	
Hypophosphataemia			
subjects affected / exposed	4 / 675 (0.59%)	2 / 336 (0.60%)	
occurrences (all)	4	3	
Hypoproteinaemia			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Hyposideraemia			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Increased appetite			
subjects affected / exposed	3 / 675 (0.44%)	0 / 336 (0.00%)	
occurrences (all)	4	0	
Iron deficiency			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	2	0	
Magnesium deficiency			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Malnutrition			
subjects affected / exposed	3 / 675 (0.44%)	0 / 336 (0.00%)	
occurrences (all)	3	0	
Metabolic acidosis			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Polydipsia			
subjects affected / exposed	2 / 675 (0.30%)	0 / 336 (0.00%)	
occurrences (all)	2	0	
Protein deficiency			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	
Type 2 diabetes mellitus			
subjects affected / exposed	2 / 675 (0.30%)	1 / 336 (0.30%)	
occurrences (all)	2	1	

Vitamin b complex deficiency			
subjects affected / exposed	0 / 675 (0.00%)	1 / 336 (0.30%)	
occurrences (all)	0	1	
Vitamin d deficiency			
subjects affected / exposed	2 / 675 (0.30%)	1 / 336 (0.30%)	
occurrences (all)	3	1	
Vitamin k deficiency			
subjects affected / exposed	1 / 675 (0.15%)	0 / 336 (0.00%)	
occurrences (all)	1	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
27 November 2012	- Amgen documentation regarding the process for determination of expectedness of adverse events for expedited reporting to regulatory agencies globally was amended - The timeline for serious adverse event reporting was changed (within 24 hours) - The Pregnancy and Lactation Reporting section was updated - The reporting of serious adverse events using the electronic serious adverse event report form was clarified
17 January 2014	- The sample size was reduced from 2000 to 1000 subjects to enhance the feasibility of study completion without compromising the integrity of the primary endpoint of the study - Language on safety data collection, recording, and reporting was updated - Language on how to address and report serious adverse events occurring outside the protocol reporting period was added

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported