



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
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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	Subject, Investigator

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
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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/m ² 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/m ² 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/m ² 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/m ² 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
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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
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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]
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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
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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]
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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
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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
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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
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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
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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
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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
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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
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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
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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
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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
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	19.1
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Reporting groups

Reporting group title	Trebananib + Paclitaxel + Carboplatin
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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
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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 occurrences (all)	1 / 675 (0.15%) 1	0 / 336 (0.00%) 0
Breast cancer subjects affected / exposed occurrences (all)	1 / 675 (0.15%) 1	0 / 336 (0.00%) 0
Cancer pain subjects affected / exposed occurrences (all)	2 / 675 (0.30%) 2	0 / 336 (0.00%) 0
Endometrial adenocarcinoma subjects affected / exposed occurrences (all)	1 / 675 (0.15%) 1	0 / 336 (0.00%) 0
Lung adenocarcinoma subjects affected / exposed occurrences (all)	1 / 675 (0.15%) 1	0 / 336 (0.00%) 0
Lung neoplasm malignant subjects affected / exposed occurrences (all)	1 / 675 (0.15%) 1	0 / 336 (0.00%) 0
Malignant ascites subjects affected / exposed occurrences (all)	2 / 675 (0.30%) 2	0 / 336 (0.00%) 0
Malignant pleural effusion subjects affected / exposed occurrences (all)	2 / 675 (0.30%) 2	0 / 336 (0.00%) 0
Metastases to lymph nodes subjects affected / exposed occurrences (all)	0 / 675 (0.00%) 0	1 / 336 (0.30%) 1
Neoplasm subjects affected / exposed occurrences (all)	1 / 675 (0.15%) 1	0 / 336 (0.00%) 0
Pancreatic neoplasm subjects affected / exposed occurrences (all)	0 / 675 (0.00%) 0	1 / 336 (0.30%) 1
Respiratory papilloma subjects affected / exposed occurrences (all)	1 / 675 (0.15%) 1	0 / 336 (0.00%) 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 occurrences (all)	4 / 675 (0.59%) 4	2 / 336 (0.60%) 3	
Sarcoidosis subjects affected / exposed occurrences (all)	0 / 675 (0.00%) 0	1 / 336 (0.30%) 1	
Social circumstances Menopause subjects affected / exposed occurrences (all)	0 / 675 (0.00%) 0	1 / 336 (0.30%) 1	
Reproductive system and breast disorders Atrophic vulvovaginitis subjects affected / exposed occurrences (all)	1 / 675 (0.15%) 1	0 / 336 (0.00%) 0	
Bartholin's cyst subjects affected / exposed occurrences (all)	1 / 675 (0.15%) 1	0 / 336 (0.00%) 0	
Bleeding anovulatory subjects affected / exposed occurrences (all)	0 / 675 (0.00%) 0	1 / 336 (0.30%) 1	
Breast cyst subjects affected / exposed occurrences (all)	1 / 675 (0.15%) 1	0 / 336 (0.00%) 0	
Breast disorder subjects affected / exposed occurrences (all)	1 / 675 (0.15%) 1	0 / 336 (0.00%) 0	
Breast hyperplasia subjects affected / exposed occurrences (all)	1 / 675 (0.15%) 1	0 / 336 (0.00%) 0	
Breast mass subjects affected / exposed occurrences (all)	3 / 675 (0.44%) 3	0 / 336 (0.00%) 0	
Breast pain subjects affected / exposed occurrences (all)	5 / 675 (0.74%) 7	3 / 336 (0.89%) 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 occurrences (all)	1 / 675 (0.15%) 1	0 / 336 (0.00%) 0	
Tearfulness subjects affected / exposed occurrences (all)	1 / 675 (0.15%) 1	0 / 336 (0.00%) 0	
Product issues Device failure subjects affected / exposed occurrences (all)	1 / 675 (0.15%) 1	0 / 336 (0.00%) 0	
Device issue subjects affected / exposed occurrences (all)	1 / 675 (0.15%) 1	0 / 336 (0.00%) 0	
Device occlusion subjects affected / exposed occurrences (all)	1 / 675 (0.15%) 1	0 / 336 (0.00%) 0	
Thrombosis in device subjects affected / exposed occurrences (all)	1 / 675 (0.15%) 1	1 / 336 (0.30%) 1	
Hepatobiliary disorders Cholelithiasis subjects affected / exposed occurrences (all)	1 / 675 (0.15%) 1	0 / 336 (0.00%) 0	
Drug-induced liver injury subjects affected / exposed occurrences (all)	0 / 675 (0.00%) 0	1 / 336 (0.30%) 1	
Hepatic function abnormal subjects affected / exposed occurrences (all)	1 / 675 (0.15%) 3	0 / 336 (0.00%) 0	
Hepatic pain subjects affected / exposed occurrences (all)	0 / 675 (0.00%) 0	1 / 336 (0.30%) 1	
Hepatic steatosis subjects affected / exposed occurrences (all)	0 / 675 (0.00%) 0	1 / 336 (0.30%) 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	
Hypertransaminaemia			
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 occurrences (all)	1 / 675 (0.15%) 1	1 / 336 (0.30%) 1
Hepatic enzyme increased subjects affected / exposed occurrences (all)	2 / 675 (0.30%) 4	2 / 336 (0.60%) 2
Hypophonesis subjects affected / exposed occurrences (all)	1 / 675 (0.15%) 1	0 / 336 (0.00%) 0
International normalised ratio increased subjects affected / exposed occurrences (all)	3 / 675 (0.44%) 4	0 / 336 (0.00%) 0
Intraocular pressure increased subjects affected / exposed occurrences (all)	4 / 675 (0.59%) 4	0 / 336 (0.00%) 0
Liver function test subjects affected / exposed occurrences (all)	1 / 675 (0.15%) 1	0 / 336 (0.00%) 0
Liver function test increased subjects affected / exposed occurrences (all)	1 / 675 (0.15%) 1	2 / 336 (0.60%) 2
Lymphocyte count decreased subjects affected / exposed occurrences (all)	3 / 675 (0.44%) 7	1 / 336 (0.30%) 6
Nerve conduction studies abnormal subjects affected / exposed occurrences (all)	1 / 675 (0.15%) 1	0 / 336 (0.00%) 0
Neutrophil count subjects affected / exposed occurrences (all)	2 / 675 (0.30%) 2	2 / 336 (0.60%) 2
Neutrophil count abnormal subjects affected / exposed occurrences (all)	0 / 675 (0.00%) 0	2 / 336 (0.60%) 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 occurrences (all)	1 / 675 (0.15%) 1	1 / 336 (0.30%) 1
Urine analysis abnormal subjects affected / exposed occurrences (all)	0 / 675 (0.00%) 0	1 / 336 (0.30%) 3
Urine output decreased subjects affected / exposed occurrences (all)	1 / 675 (0.15%) 1	2 / 336 (0.60%) 2
Urine output increased subjects affected / exposed occurrences (all)	2 / 675 (0.30%) 2	0 / 336 (0.00%) 0
Urine protein, quantitative subjects affected / exposed occurrences (all)	1 / 675 (0.15%) 1	0 / 336 (0.00%) 0
Vitamin d decreased subjects affected / exposed occurrences (all)	0 / 675 (0.00%) 0	1 / 336 (0.30%) 1
Waist circumference increased subjects affected / exposed occurrences (all)	1 / 675 (0.15%) 1	0 / 336 (0.00%) 0
Weight decreased subjects affected / exposed occurrences (all)	28 / 675 (4.15%) 52	19 / 336 (5.65%) 41
Weight increased subjects affected / exposed occurrences (all)	46 / 675 (6.81%) 107	19 / 336 (5.65%) 27
White blood cell analysis abnormal subjects affected / exposed occurrences (all)	1 / 675 (0.15%) 1	0 / 336 (0.00%) 0
White blood cell count subjects affected / exposed occurrences (all)	1 / 675 (0.15%) 1	0 / 336 (0.00%) 0
White blood cell count abnormal subjects affected / exposed occurrences (all)	1 / 675 (0.15%) 1	1 / 336 (0.30%) 1

White blood cell count decreased subjects affected / exposed occurrences (all)	48 / 675 (7.11%) 199	19 / 336 (5.65%) 87	
White blood cell count increased subjects affected / exposed occurrences (all)	2 / 675 (0.30%) 2	0 / 336 (0.00%) 0	
White blood cells urine positive subjects affected / exposed occurrences (all)	1 / 675 (0.15%) 1	1 / 336 (0.30%) 1	
Injury, poisoning and procedural complications			
Animal scratch subjects affected / exposed occurrences (all)	0 / 675 (0.00%) 0	1 / 336 (0.30%) 1	
Arthropod bite subjects affected / exposed occurrences (all)	1 / 675 (0.15%) 1	4 / 336 (1.19%) 4	
Ankle fracture subjects affected / exposed occurrences (all)	1 / 675 (0.15%) 1	0 / 336 (0.00%) 0	
Arthropod sting subjects affected / exposed occurrences (all)	1 / 675 (0.15%) 1	0 / 336 (0.00%) 0	
Chest crushing subjects affected / exposed occurrences (all)	0 / 675 (0.00%) 0	1 / 336 (0.30%) 1	
Contusion subjects affected / exposed occurrences (all)	16 / 675 (2.37%) 23	11 / 336 (3.27%) 14	
Contrast media reaction subjects affected / exposed occurrences (all)	2 / 675 (0.30%) 2	1 / 336 (0.30%) 1	
Epicondylitis subjects affected / exposed occurrences (all)	0 / 675 (0.00%) 0	1 / 336 (0.30%) 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 occurrences (all)	1 / 675 (0.15%) 1	1 / 336 (0.30%) 1
Procedural nausea subjects affected / exposed occurrences (all)	10 / 675 (1.48%) 11	5 / 336 (1.49%) 5
Procedural pain subjects affected / exposed occurrences (all)	43 / 675 (6.37%) 46	22 / 336 (6.55%) 22
Rib fracture subjects affected / exposed occurrences (all)	1 / 675 (0.15%) 1	1 / 336 (0.30%) 1
Seroma subjects affected / exposed occurrences (all)	1 / 675 (0.15%) 1	0 / 336 (0.00%) 0
Skin abrasion subjects affected / exposed occurrences (all)	3 / 675 (0.44%) 3	1 / 336 (0.30%) 3
Stoma site haemorrhage subjects affected / exposed occurrences (all)	0 / 675 (0.00%) 0	1 / 336 (0.30%) 1
Stoma site inflammation subjects affected / exposed occurrences (all)	1 / 675 (0.15%) 1	0 / 336 (0.00%) 0
Stoma site irritation subjects affected / exposed occurrences (all)	0 / 675 (0.00%) 0	1 / 336 (0.30%) 1
Stoma site reaction subjects affected / exposed occurrences (all)	1 / 675 (0.15%) 1	0 / 336 (0.00%) 0
Thermal burn subjects affected / exposed occurrences (all)	1 / 675 (0.15%) 1	0 / 336 (0.00%) 0
Tooth fracture subjects affected / exposed occurrences (all)	1 / 675 (0.15%) 1	1 / 336 (0.30%) 1

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

subjects affected / exposed occurrences (all)	1 / 675 (0.15%) 1	0 / 336 (0.00%) 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 occurrences (all)	0 / 675 (0.00%) 0	1 / 336 (0.30%) 1	
Ventricular extrasystoles subjects affected / exposed occurrences (all)	3 / 675 (0.44%) 3	1 / 336 (0.30%) 1	
Ventricular flutter subjects affected / exposed occurrences (all)	1 / 675 (0.15%) 1	0 / 336 (0.00%) 0	
Ventricular tachycardia subjects affected / exposed occurrences (all)	1 / 675 (0.15%) 1	0 / 336 (0.00%) 0	
Nervous system disorders			
Amnesia subjects affected / exposed occurrences (all)	5 / 675 (0.74%) 5	1 / 336 (0.30%) 1	
Anosmia subjects affected / exposed occurrences (all)	1 / 675 (0.15%) 1	0 / 336 (0.00%) 0	
Aphasia subjects affected / exposed occurrences (all)	2 / 675 (0.30%) 2	1 / 336 (0.30%) 1	
Aphonia subjects affected / exposed occurrences (all)	1 / 675 (0.15%) 1	1 / 336 (0.30%) 1	
Ataxia subjects affected / exposed occurrences (all)	3 / 675 (0.44%) 4	0 / 336 (0.00%) 0	
Aura subjects affected / exposed occurrences (all)	1 / 675 (0.15%) 1	0 / 336 (0.00%) 0	
Balance disorder subjects affected / exposed occurrences (all)	3 / 675 (0.44%) 3	4 / 336 (1.19%) 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 occurrences (all)	1 / 675 (0.15%) 1	1 / 336 (0.30%) 1
Coagulopathy subjects affected / exposed occurrences (all)	1 / 675 (0.15%) 1	0 / 336 (0.00%) 0
Febrile neutropenia subjects affected / exposed occurrences (all)	5 / 675 (0.74%) 5	2 / 336 (0.60%) 2
Haematotoxicity subjects affected / exposed occurrences (all)	0 / 675 (0.00%) 0	1 / 336 (0.30%) 1
Hypercoagulation subjects affected / exposed occurrences (all)	1 / 675 (0.15%) 1	0 / 336 (0.00%) 0
Hypochromasia subjects affected / exposed occurrences (all)	0 / 675 (0.00%) 0	1 / 336 (0.30%) 1
Increased tendency to bruise subjects affected / exposed occurrences (all)	2 / 675 (0.30%) 2	1 / 336 (0.30%) 1
Iron deficiency anaemia subjects affected / exposed occurrences (all)	1 / 675 (0.15%) 2	0 / 336 (0.00%) 0
Leukocytosis subjects affected / exposed occurrences (all)	0 / 675 (0.00%) 0	2 / 336 (0.60%) 2
Leukopenia subjects affected / exposed occurrences (all)	116 / 675 (17.19%) 466	58 / 336 (17.26%) 205
Lymph node pain subjects affected / exposed occurrences (all)	1 / 675 (0.15%) 1	0 / 336 (0.00%) 0
Lymphadenitis subjects affected / exposed occurrences (all)	1 / 675 (0.15%) 1	0 / 336 (0.00%) 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 occurrences (all)	0 / 675 (0.00%) 0	1 / 336 (0.30%) 1	
Tinnitus subjects affected / exposed occurrences (all)	26 / 675 (3.85%) 28	6 / 336 (1.79%) 9	
Vertigo subjects affected / exposed occurrences (all)	21 / 675 (3.11%) 25	4 / 336 (1.19%) 8	
Vertigo positional subjects affected / exposed occurrences (all)	1 / 675 (0.15%) 1	1 / 336 (0.30%) 1	
Eye disorders			
Age-related macular degeneration subjects affected / exposed occurrences (all)	0 / 675 (0.00%) 0	1 / 336 (0.30%) 1	
Amblyopia subjects affected / exposed occurrences (all)	1 / 675 (0.15%) 1	0 / 336 (0.00%) 0	
Asthenopia subjects affected / exposed occurrences (all)	0 / 675 (0.00%) 0	3 / 336 (0.89%) 3	
Blepharospasm subjects affected / exposed occurrences (all)	1 / 675 (0.15%) 1	0 / 336 (0.00%) 0	
Cataract subjects affected / exposed occurrences (all)	5 / 675 (0.74%) 6	2 / 336 (0.60%) 2	
Chalazion subjects affected / exposed occurrences (all)	1 / 675 (0.15%) 1	2 / 336 (0.60%) 2	
Conjunctival haemorrhage subjects affected / exposed occurrences (all)	1 / 675 (0.15%) 1	2 / 336 (0.60%) 3	
Conjunctival oedema subjects affected / exposed occurrences (all)	1 / 675 (0.15%) 2	0 / 336 (0.00%) 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
Onychoclasia		
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 occurrences (all)	2 / 675 (0.30%) 2	0 / 336 (0.00%) 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 occurrences (all)	16 / 675 (2.37%) 20	12 / 336 (3.57%) 15	
Urinary retention subjects affected / exposed occurrences (all)	6 / 675 (0.89%) 6	0 / 336 (0.00%) 0	
Urinary tract disorder subjects affected / exposed occurrences (all)	3 / 675 (0.44%) 5	0 / 336 (0.00%) 0	
Urinary tract pain subjects affected / exposed occurrences (all)	2 / 675 (0.30%) 2	0 / 336 (0.00%) 0	
Urine abnormality subjects affected / exposed occurrences (all)	1 / 675 (0.15%) 1	0 / 336 (0.00%) 0	
Endocrine disorders			
Cushing's syndrome subjects affected / exposed occurrences (all)	0 / 675 (0.00%) 0	1 / 336 (0.30%) 1	
Goitre subjects affected / exposed occurrences (all)	2 / 675 (0.30%) 2	0 / 336 (0.00%) 0	
Hyperparathyroidism primary subjects affected / exposed occurrences (all)	1 / 675 (0.15%) 1	0 / 336 (0.00%) 0	
Hyperthyroidism subjects affected / exposed occurrences (all)	0 / 675 (0.00%) 0	1 / 336 (0.30%) 1	
Hypothyroidism subjects affected / exposed occurrences (all)	4 / 675 (0.59%) 4	4 / 336 (1.19%) 4	
Thyroid cyst subjects affected / exposed occurrences (all)	2 / 675 (0.30%) 2	0 / 336 (0.00%) 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 occurrences (all)	1 / 675 (0.15%) 1	0 / 336 (0.00%) 0
Decreased appetite subjects affected / exposed occurrences (all)	175 / 675 (25.93%) 278	89 / 336 (26.49%) 143
Dehydration subjects affected / exposed occurrences (all)	34 / 675 (5.04%) 52	13 / 336 (3.87%) 14
Diabetes mellitus subjects affected / exposed occurrences (all)	2 / 675 (0.30%) 2	1 / 336 (0.30%) 1
Fluid imbalance subjects affected / exposed occurrences (all)	1 / 675 (0.15%) 1	0 / 336 (0.00%) 0
Fluid retention subjects affected / exposed occurrences (all)	3 / 675 (0.44%) 3	0 / 336 (0.00%) 0
Food craving subjects affected / exposed occurrences (all)	0 / 675 (0.00%) 0	1 / 336 (0.30%) 1
Gout subjects affected / exposed occurrences (all)	1 / 675 (0.15%) 2	1 / 336 (0.30%) 1
Hyper hdl cholesterolaemia subjects affected / exposed occurrences (all)	0 / 675 (0.00%) 0	1 / 336 (0.30%) 1
Hypercalcaemia subjects affected / exposed occurrences (all)	4 / 675 (0.59%) 4	1 / 336 (0.30%) 1
Hypercholesterolaemia subjects affected / exposed occurrences (all)	8 / 675 (1.19%) 8	1 / 336 (0.30%) 1
Hyperglycaemia subjects affected / exposed occurrences (all)	30 / 675 (4.44%) 57	12 / 336 (3.57%) 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 occurrences (all)	0 / 675 (0.00%) 0	1 / 336 (0.30%) 1	
Vitamin d deficiency subjects affected / exposed occurrences (all)	2 / 675 (0.30%) 3	1 / 336 (0.30%) 1	
Vitamin k deficiency subjects affected / exposed occurrences (all)	1 / 675 (0.15%) 1	0 / 336 (0.00%) 0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
27 November 2012	<ul style="list-style-type: none">- 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	<ul style="list-style-type: none">- 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