



Clinical trial results:

A Phase 3, Randomized, Double-blind Trial of Weekly Paclitaxel Plus AMG 386 or Placebo in Women With Recurrent Partially Platinum Sensitive or Resistant Epithelial Ovarian, Primary Peritoneal or Fallopian Tube Cancers

Summary

EudraCT number	2010-019821-32
Trial protocol	FR ES PT CZ SI GR SE LV EE IT BG GB BE
Global end of trial date	16 December 2016

Results information

Result version number	v1 (current)
This version publication date	23 December 2017
First version publication date	23 December 2017

Trial information

Trial identification

Sponsor protocol code	20090508
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01204749
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	16 December 2016
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	16 December 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to determine if paclitaxel plus trebananib is superior to paclitaxel plus placebo, as measured by progression-free survival (PFS), defined as the time from randomization to the earliest of the dates of first radiologic disease progression per Response Evaluation Criteria in Solid Tumors version 1.1 (RECIST 1.1) with modifications or death from any cause, in subjects with recurrent partially platinum-sensitive or -resistant epithelial ovarian, primary peritoneal, or fallopian tube cancers.

Protection of trial subjects:

This study was conducted in accordance with United States Food and Drug Administration (FDA) regulations/guidelines set forth in 21 CFR Parts 11, 50, 54, 56, and 312 and International Conference on Harmonisation (ICH) Good Clinical Practice (GCP) regulations/guidelines.

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	10 November 2010
Long term follow-up planned	Yes
Long term follow-up rationale	Efficacy
Long term follow-up duration	60 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Canada: 104
Country: Number of subjects enrolled	United States: 80
Country: Number of subjects enrolled	Australia: 20
Country: Number of subjects enrolled	Belgium: 14
Country: Number of subjects enrolled	France: 110
Country: Number of subjects enrolled	Greece: 38
Country: Number of subjects enrolled	Italy: 53
Country: Number of subjects enrolled	Portugal: 13
Country: Number of subjects enrolled	Spain: 104
Country: Number of subjects enrolled	Sweden: 10
Country: Number of subjects enrolled	Switzerland: 11

Country: Number of subjects enrolled	United Kingdom: 9
Country: Number of subjects enrolled	Brazil: 11
Country: Number of subjects enrolled	Bulgaria: 8
Country: Number of subjects enrolled	Chile: 11
Country: Number of subjects enrolled	Croatia: 3
Country: Number of subjects enrolled	Czech Republic: 9
Country: Number of subjects enrolled	Estonia: 6
Country: Number of subjects enrolled	Hong Kong: 3
Country: Number of subjects enrolled	India: 27
Country: Number of subjects enrolled	Israel: 15
Country: Number of subjects enrolled	Japan: 57
Country: Number of subjects enrolled	Korea, Republic of: 28
Country: Number of subjects enrolled	Latvia: 25
Country: Number of subjects enrolled	Malaysia: 11
Country: Number of subjects enrolled	Mexico: 20
Country: Number of subjects enrolled	Peru: 6
Country: Number of subjects enrolled	Poland: 34
Country: Number of subjects enrolled	Romania: 7
Country: Number of subjects enrolled	Russian Federation: 56
Country: Number of subjects enrolled	Slovenia: 5
Country: Number of subjects enrolled	South Africa: 11
Worldwide total number of subjects	919
EEA total number of subjects	448

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)	651
From 65 to 84 years	268
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This study was conducted at 179 centers in 32 countries from November 2010 to December 2016.

Pre-assignment

Screening details:

A total of 1092 subjects were screened and 919 subjects randomized in a 1:1 ratio. Randomization was stratified based on platinum-free interval (PFI) (PFI ≥ 0 and ≤ 6 months vs PFI > 6 months and ≤ 12 months), presence/absence of measurable disease, and region (North America, Western Europe/Australia, rest of the world [ROW]).

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, Monitor

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Participants received paclitaxel 80 mg/m² as an intravenous (IV) infusion on weeks 1, 2, and 3 of each 4-week cycle plus placebo to trebananib by IV infusion once every week until disease progression, unacceptable toxicity, withdrawal of consent, or death.

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 as an IV infusion via an infusion pump or gravity over 30 to 60 minutes once a week.

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

Dosage and administration details:

Administered as an IV infusion over 1 hour on weeks 1, 2, and 3 of each 4-week cycle.

Arm title	Trebananib
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Arm description:

Participants received paclitaxel 80 mg/m² as an intravenous (IV) infusion on weeks 1, 2, and 3 of each 4-week cycle plus trebananib 15 mg/kg by IV infusion once every week until disease progression, unacceptable toxicity, withdrawal of consent, or death.

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:

Administered as an IV infusion via an infusion pump or gravity over 30 to 60 minutes once a week.

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

Dosage and administration details:

Administered as an IV infusion over 1 hour on weeks 1, 2, and 3 of each 4-week cycle.

Number of subjects in period 1	Placebo	Trebananib
Started	458	461
Received trebananib/placebo	454	459
Completed	2	0
Not completed	456	461
Consent withdrawn by subject	16	24
Death	392	399
Other	41	29
Lost to follow-up	7	9

Baseline characteristics

Reporting groups

Reporting group title	Placebo
Reporting group description:	
Participants received paclitaxel 80 mg/m ² as an intravenous (IV) infusion on weeks 1, 2, and 3 of each 4-week cycle plus placebo to trebananib by IV infusion once every week until disease progression, unacceptable toxicity, withdrawal of consent, or death.	
Reporting group title	Trebananib
Reporting group description:	
Participants received paclitaxel 80 mg/m ² as an intravenous (IV) infusion on weeks 1, 2, and 3 of each 4-week cycle plus trebananib 15 mg/kg by IV infusion once every week until disease progression, unacceptable toxicity, withdrawal of consent, or death.	

Reporting group values	Placebo	Trebananib	Total
Number of subjects	458	461	919
Age Categorical			
Units: Subjects			
Adults (18-64 years)	333	318	651
From 65-84 years	125	143	268
85 years and over	0	0	0
Age Continuous			
Units: years			
arithmetic mean	57.9	58.8	-
standard deviation	± 10.7	± 1.4	-
Gender Categorical			
Units: Subjects			
Female	458	461	919
Male	0	0	0
Race			
Units: Subjects			
American Indian or Alaska Native	1	0	1
Asian	82	58	140
Black (or African American)	7	6	13
Native Hawaiian or Other Pacific Islander	1	1	2
White	363	387	750
Other	4	9	13
Primary Tumor Type			
Units: Subjects			
Fallopian Tube Cancer	15	14	29
Ovarian Cancer	419	423	842
Primary Peritoneal Carcinoma	24	24	48
Stratification: Measurable Disease at Baseline			
Units: Subjects			
Yes	436	438	874
No	22	23	45
Stratification Factor: Region			
Units: Subjects			

North America	91	93	184
Western Europe/Australia	237	238	475
Rest of the World	130	130	260
Stratification Status: Platinum-free Interval Status			
Platinum-free interval (PFI) is defined as the time from the last dose of the most recent platinum agent until the first date disease progression was noted during or following discontinuation of the prior platinum agent.			
Units: Subjects			
PFI ≥ 0 to ≤ 6 months	229	232	461
PFI > 6 months and ≤ 12 months	229	229	458

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description: Participants received paclitaxel 80 mg/m ² as an intravenous (IV) infusion on weeks 1, 2, and 3 of each 4-week cycle plus placebo to trebananib by IV infusion once every week until disease progression, unacceptable toxicity, withdrawal of consent, or death.	
Reporting group title	Trebananib
Reporting group description: Participants received paclitaxel 80 mg/m ² as an intravenous (IV) infusion on weeks 1, 2, and 3 of each 4-week cycle plus trebananib 15 mg/kg by IV infusion once every week until disease progression, unacceptable toxicity, withdrawal of consent, or death.	

Primary: Progression-free Survival

End point title	Progression-free Survival
End point description: Progression-free survival (PFS) is defined as the time from the date of randomization to the earliest of the dates of first objective disease progression or death from any cause. The determination of radiologic disease progression was based on investigator assessments, per RECIST 1.1 with modifications. Participants not meeting PFS criteria by the analysis data cutoff date were censored at their last evaluable radiologic disease assessment date. Events of radiographic progression per RECIST 1.1 with modifications that occurred after initiation of subsequent anticancer therapy were not considered PFS events and were censored at the last evaluable radiographic tumor assessment prior to initiation of subsequent anticancer therapy. Deaths occurring after initiation of subsequent anticancer therapy were considered PFS events.	
End point type	Primary
End point timeframe: From randomization to the data cut-off date; median follow-up time was 17.7 months.	

End point values	Placebo	Trebananib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	458	461		
Units: months				
median (confidence interval 95%)	5.4 (4.8 to 5.5)	7.4 (7.0 to 7.8)		

Statistical analyses

Statistical analysis title	Primary Analysis
Comparison groups	Placebo v Trebananib

Number of subjects included in analysis	919
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 ^[1]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.72
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.63
upper limit	0.82

Notes:

[1] - Log rank test stratified by PFI status and region

Secondary: Overall Survival

End point title	Overall Survival
End point description:	
Overall survival was a key secondary endpoint and was defined as the time from the randomization date to the date of death from any cause. Subjects known to be alive prior to the data cutoff date were censored at the last contact prior to the cutoff date. Subjects known to be alive or dead after the data cutoff date were censored at the data cutoff date.	
End point type	Secondary
End point timeframe:	
From randomization to the data cut-off date; median follow-up time was 17.7 months.	

End point values	Placebo	Trebananib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	458	461		
Units: months				
median (confidence interval 95%)	18.3 (16.2 to 20.4)	19.3 (17.7 to 21.4)		

Statistical analyses

Statistical analysis title	Analysis of Overall Survival
Comparison groups	Placebo v Trebananib
Number of subjects included in analysis	919
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.71 ^[2]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.03

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.89
upper limit	1.18

Notes:

[2] - Log rank test stratified by PFI status and region.

Secondary: Objective Response Rate

End point title	Objective Response Rate
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End point description:

Objective response rate (ORR) was defined as the incidence of either a complete response (CR) or partial response (PR) while on study, as defined in RECIST 1.1 with modifications. Confirmation for PR and CR was not required. All subjects who did not meet the criteria for objective response by the analysis cutoff date were considered non-responders. Only subjects with measurable disease at baseline were included in the analysis of ORR.

End point type	Secondary
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End point timeframe:

From randomization to the data cut-off date; median follow-up time was 17.7 months.

End point values	Placebo	Trebananib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	433	436		
Units: percentage of participants				
number (confidence interval 95%)	31.4 (27.1 to 36.0)	39.9 (35.3 to 44.7)		

Statistical analyses

Statistical analysis title	Analysis of Objective Response Rate
Comparison groups	Placebo v Trebananib
Number of subjects included in analysis	869
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.009 ^[3]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	1.465
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.102
upper limit	1.948

Notes:

[3] - Cochran-Mantel-Haenszel test adjusted for platinum sensitivity status.

Secondary: Duration of Response

End point title	Duration of Response
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End point description:

Duration of response (DOR) was defined as the time from the first objective response to disease progression per RECIST 1.1 with modifications or death due to any cause. Subjects not meeting criteria for disease progression per RECIST 1.1 with modifications by the analysis data cutoff date were censored at their last evaluable disease assessment date.

The analysis of DOR was conducted on the subset of subjects with measurable disease at baseline who experienced an objective response during the study.

End point type	Secondary
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End point timeframe:

From randomization to the data cut-off date; median follow-up time was 17.7 months.

End point values	Placebo	Trebananib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	136	174		
Units: months				
median (confidence interval 95%)	5.1 (3.8 to 5.6)	7.4 (5.6 to 9.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: CA-125 Response Rate

End point title	CA-125 Response Rate
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End point description:

CA-125 is a tumor marker to monitor response to treatment and recurrence in ovarian cancer. CA-125 response was evaluated as a secondary endpoint among subjects with baseline CA-125 $\geq 2 \times$ upper limit of normal (ULN) and was defined as a $\geq 50\%$ reduction in CA-125 levels from baseline according to the Gynecologic Cancer Intergroup (GCIg) criteria. All subjects evaluable for CA-125 response that did not meet the criteria for a CA-125 response were considered non-responders.

End point type	Secondary
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End point timeframe:

From randomization to the data cut-off date; median follow-up time was 17.7 months.

End point values	Placebo	Trebananib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	371	366		
Units: percentage of participants				
number (confidence interval 95%)	48.5 (43.3 to 53.7)	56.3 (51.0 to 61.4)		

Statistical analyses

Statistical analysis title	Analysis of CA-125 Response
Comparison groups	Placebo v Trebananib
Number of subjects included in analysis	737
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.029 ^[4]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	1.3943
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.035
upper limit	1.878

Notes:

[4] - Cochran-Mantel-Haenszel test adjusted for platinum sensitivity status.

Secondary: Number of Participants with Adverse Events

End point title	Number of Participants with Adverse Events
End point description:	
Adverse events (AEs) were graded using the Common Terminology Criteria for Adverse Events (CTCAE) version 3.0. Trebananib/placebo-related or paclitaxel-related adverse events are those events for which the investigator considered there to be a reasonable possibility that the event may have been caused by the study treatment, trebananib/placebo or paclitaxel, respectively. Participants are analyzed according to treatment actually received.	
End point type	Secondary
End point timeframe:	
From first dose of any study drug up to 30 days after the last dose; median duration was 134 days for placebo and 156 days for trebananib.	

End point values	Placebo	Trebananib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	452	461		
Units: participants				
Any adverse event	434	449		
AE Grade \geq 3	255	280		
AE Grade \geq 4	57	55		
Serious adverse events (SAE)	138	168		
Leading to discontinuation of trebananib/placebo	34	102		
Leading to discontinuation of paclitaxel	47	89		
Leading to discontinuation from study treatment	19	54		
Fatal adverse events	20	26		
Trebananib/placebo related AEs	310	366		
Trebananib/placebo related AE Grade \geq 3	85	149		
Trebananib/placebo related AE Grade \geq 4	14	14		

Trebananib/placebo related SAE	31	57		
Paclitaxel related adverse events	388	387		
Paclitaxel related AE Grade ≥ 3	106	120		
Paclitaxel related AE Grade ≥ 4	11	9		
Paclitaxel related SAE	24	32		

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Observed Serum Concentration (Cmax) of Trebananib

End point title	Maximum Observed Serum Concentration (Cmax) of Trebananib ^[5]
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End point description:

End point type	Secondary
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End point timeframe:

Weeks 1 and 5 at the end of infusion

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 conducted for the trebananib treatment group

End point values	Trebananib			
Subject group type	Reporting group			
Number of subjects analysed	397			
Units: $\mu\text{g/mL}$				
arithmetic mean (standard deviation)				
Week 1 (n = 397)	310 (\pm 119)			
Week 5 (n = 288)	351 (\pm 105)			

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 ^[6]
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End point description:

End point type	Secondary
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End point timeframe:

Weeks 2, 5 and 9, predose

Notes:

[6] - 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 conducted for the trebananib treatment group

End point values	Trebananib			
Subject group type	Reporting group			
Number of subjects analysed	405			
Units: µg/mL				
arithmetic mean (standard deviation)				
Week 2 (n = 405)	14.6 (± 7.69)			
Week 5 (n = 323)	27.5 (± 14.3)			
Week 9 (n = 284)	29.6 (± 16.9)			

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:	
Blood samples were tested for anti-trebananib binding antibodies using a validated biosensore Biacore® immunoassay. Samples with positive binding antibody results were further tested for the neutralizing activity of the antibody using a validated electrochemiluminescence receptor-binding assay. Participants were considered positive for developing antibodies if they had a negative or no result at baseline and a positive result post-baseline.	
End point type	Secondary
End point timeframe:	
Day 1 of weeks 1 and 9 and 30 days after last dose	

End point values	Placebo	Trebananib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	410 ^[7]	409 ^[8]		
Units: participants				
Binding Antibody Positive	14	46		
Neutralizing Antibody Positive	1	0		

Notes:

[7] - Subjects with a post-baseline result

[8] - Subjects with a post-baseline result

Statistical analyses

No statistical analyses for this end point

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

End point title	Change from Baseline in Functional Assessment of Cancer Therapy – Ovary (FACT-O) Summary Score
End point description:	
The FACT-O evaluates the health-related quality of life (HRQOL) and symptoms in patients with ovarian cancer. It consists of the FACT-G, a 27 item general cancer questionnaire and a 12-item ovarian cancer-specific subscale (OCS). Each item is scored by the participant on a scale from 0 (not at all true) to 4 (very much true). The total score ranges from 0 to 156; a higher total score indicates better quality of	

life or less severe symptoms.

The patient-reported outcomes (PRO) analysis set is defined as a subset of randomized subjects who have a baseline PRO assessment and at least one post-baseline PRO assessment prior to disease progression

End point type	Secondary
End point timeframe:	
Baseline and Weeks 5, 9, 13, 17, 25, 33, 41, 49, 57, 65, 73, 81, and the safety follow-up visit 30 days after last dose.	

End point values	Placebo	Trebananib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	414	398		
Units: units on a scale				
arithmetic mean (standard deviation)				
Week 5 (n = 391, 375)	-0.102 (± 13.085)	-2.241 (± 14.249)		
Week 9 (n = 306, 310)	-0.034 (± 12.887)	-1.746 (± 15.602)		
Week 13 (n = 256, 288)	-0.407 (± 14.503)	-2.366 (± 17.063)		
Week 17 (n = 223, 247)	-0.058 (± 15.304)	-2.209 (± 17.859)		
Week 25 (n = 134, 168)	-1.470 (± 15.015)	-2.532 (± 16.446)		
Week 33 (n = 81, 111)	0.579 (± 16.359)	-2.815 (± 17.335)		
Week 41 (n = 53, 69)	0.469 (± 16.854)	-2.871 (± 18.702)		
Week 49 (n = 34, 51)	4.849 (± 17.059)	-2.281 (± 18.702)		
Week 57 (n = 25, 36)	2.448 (± 15.926)	-3.392 (± 16.151)		
Week 65 (n = 20, 25)	1.203 (± 12.802)	-3.585 (± 18.792)		
Week 73 (n = 14, 25)	1.104 (± 14.694)	-3.390 (± 15.786)		
Week 81 (n = 14, 18)	0.694 (± 13.535)	0.185 (± 15.474)		
Safety follow-up (n = 24, 72)	0.557 (± 18.210)	-13.871 (± 17.397)		

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.

End point type	Secondary
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End point timeframe:

Baseline and Weeks 5, 9, 13, 17, 25, 33, 41, 49, 57, 65, 73, 81, and the safety follow-up visit 30 days after last dose.

End point values	Placebo	Trebananib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	418	407		
Units: units on a scale				
arithmetic mean (standard deviation)				
Week 5 (n = 397, 386)	-0.005 (± 4.834)	-1.105 (± 4.907)		
Week 9 (n = 312, 318)	-0.081 (± 4.815)	-0.652 (± 5.218)		
Week 13 (n = 261, 295)	-0.117 (± 5.038)	-0.674 (± 5.614)		
Week 17 (n = 228, 253)	-0.303 (± 5.190)	-0.482 (± 5.695)		
Week 25 (n = 137, 172)	-0.816 (± 4.826)	-0.709 (± 5.451)		
Week 33 (n = 83, 114)	-0.351 (± 5.616)	-0.989 (± 5.131)		
Week 41 (n = 54, 71)	-0.891 (± 5.704)	-1.211 (± 5.422)		
Week 49 (n = 35, 51)	0.384 (± 5.999)	-1.340 (± 6.740)		
Week 57 (n = 26, 38)	-0.634 (± 4.040)	-0.272 (± 3.996)		
Week 65 (n = 22, 27)	-0.831 (± 4.821)	-1.407 (± 4.849)		
Week 73 (n = 14, 25)	-0.027 (± 5.747)	-0.780 (± 4.227)		
Week 81 (n = 14, 18)	0.194 (± 4.329)	-0.311 (± 3.684)		
Safety follow-up (n = 24, 74)	0.443 (± 5.641)	-3.557 (± 5.894)		

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.

End point type	Secondary
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End point timeframe:

Baseline and Weeks 5, 9, 13, 17, 25, 33, 41, 49, 57, 65, 73, 81, and the safety follow-up visit 30 days after last dose.

End point values	Placebo	Trebananib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	412	379		
Units: units on a scale				
arithmetic mean (standard deviation)				
Week 5 (n = 383, 351)	0.022 (± 0.202)	-0.026 (± 0.215)		
Week 9 (n = 304, 296)	0.028 (± 0.208)	-0.008 (± 0.244)		
Week 13 (n = 256, 277)	0.020 (± 0.198)	-0.025 (± 0.245)		
Week 17 (n = 224, 233)	0.012 (± 0.208)	-0.011 (± 0.228)		
Week 25 (n = 133, 162)	0.018 (± 0.190)	-0.025 (± 0.225)		
Week 33 (n = 80, 109)	0.007 (± 0.219)	-0.031 (± 0.226)		
Week 41 (n = 52, 66)	0.007 (± 0.225)	-0.030 (± 0.159)		
Week 49 (n = 34, 46)	-0.042 (± 0.189)	-0.003 (± 0.217)		
Week 57 (n = 25, 34)	-0.032 (± 0.228)	-0.127 (± 0.245)		
Week 65 (n = 20, 22)	-0.056 (± 0.250)	-0.041 (± 0.242)		
Week 73 (n = 12, 22)	-0.160 (± 0.355)	-0.099 (± 0.244)		
Week 81 (n = 11, 15)	-0.134 (± 0.294)	-0.033 (± 0.159)		
Safety follow-up (n = 23, 71)	-0.006 (± 0.157)	-0.192 (± 0.317)		

Statistical analyses

No statistical analyses for this end point

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

End point title	Change from Baseline in EQ-5D Visual Analogue Scale Score
End point description:	
<p>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).</p> <p>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.</p> <p>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.</p>	
End point type	Secondary
End point timeframe:	
Baseline and Weeks 5, 9, 13, 17, 25, 33, 41, 49, 57, 65, 73, 81, and the safety follow-up visit 30 days after last dose.	

End point values	Placebo	Trebananib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	408	392		
Units: units on a scale				
arithmetic mean (standard deviation)				
Week 5 (n = 378, 366)	0.669 (± 14.875)	-2.210 (± 15.996)		
Week 9 (n = 297, 301)	0.953 (± 15.678)	0.189 (± 17.358)		
Week 13 (n = 254, 283)	0.614 (± 16.461)	-1.774 (± 18.669)		
Week 17 (n = 220, 240)	1.105 (± 18.252)	-0.542 (± 19.540)		
Week 25 (n = 131, 160)	-0.557 (± 20.135)	0.813 (± 17.777)		
Week 33 (n = 79, 111)	-0.291 (± 17.658)	0.946 (± 22.109)		
Week 41 (n = 52, 69)	1.481 (± 18.584)	0.681 (± 18.958)		
Week 49 (n = 34, 48)	2.059 (± 14.851)	3.458 (± 21.088)		
Week 57 (n = 25, 36)	-0.120 (± 14.380)	-4.028 (± 24.193)		
Week 65 (n = 20, 27)	3.000 (± 16.173)	5.667 (± 20.543)		
Week 73 (n = 14, 24)	4.357 (± 19.033)	3.125 (± 15.663)		
Week 81 (n = 13, 19)	3.308 (± 15.623)	2.526 (± 15.890)		
Safety follow-up (n = 24, 69)	-0.708 (± 26.104)	-8.130 (± 20.356)		

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 until 30 days after last dose. Median duration was 134 days for placebo and 156 days for trebananib.

Adverse event reporting additional description:

Five subjects (3 randomized to trebananib and 2 randomized to placebo) received at least 1 incorrect dose of investigational product during the study. These subjects are characterized in the safety population under the treatment they actually received rather than the treatment they were randomized to receive.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
Dictionary version	19.1

Reporting groups

Reporting group title	Placebo + Paclitaxel
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Reporting group description:

Participants received paclitaxel 80 mg/m² as an intravenous (IV) infusion on weeks 1, 2, and 3 of each 4-week cycle plus placebo to trebananib by IV infusion once every week until disease progression, unacceptable toxicity, withdrawal of consent, or death.

Reporting group title	Trebananib + Paclitaxel
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Reporting group description:

Participants received paclitaxel 80 mg/m² as an intravenous (IV) infusion on weeks 1, 2, and 3 of each 4-week cycle plus trebananib 15 mg/kg by IV infusion once every week until disease progression, unacceptable toxicity, withdrawal of consent, or death.

Serious adverse events	Placebo + Paclitaxel	Trebananib + Paclitaxel	
Total subjects affected by serious adverse events			
subjects affected / exposed	138 / 452 (30.53%)	168 / 461 (36.44%)	
number of deaths (all causes)	388	402	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer female			
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cancer pain			
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fallopian tube cancer			

subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Infected neoplasm			
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malignant ascites			
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malignant peritoneal neoplasm			
subjects affected / exposed	0 / 452 (0.00%)	2 / 461 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malignant pleural effusion			
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastases to bone			
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastases to central nervous system			
subjects affected / exposed	1 / 452 (0.22%)	2 / 461 (0.43%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 0	
Metastases to pelvis			
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastases to peritoneum			

subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Metastatic neoplasm			
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oncologic complication			
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ovarian cancer			
subjects affected / exposed	6 / 452 (1.33%)	9 / 461 (1.95%)	
occurrences causally related to treatment / all	0 / 6	0 / 9	
deaths causally related to treatment / all	0 / 6	0 / 8	
Ovarian cancer metastatic			
subjects affected / exposed	1 / 452 (0.22%)	1 / 461 (0.22%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Pleural mesothelioma			
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	1 / 452 (0.22%)	3 / 461 (0.65%)	
occurrences causally related to treatment / all	1 / 1	2 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertension			
subjects affected / exposed	0 / 452 (0.00%)	2 / 461 (0.43%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypotension			

subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemia			
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Jugular vein thrombosis			
subjects affected / exposed	0 / 452 (0.00%)	2 / 461 (0.43%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphoedema			
subjects affected / exposed	1 / 452 (0.22%)	1 / 461 (0.22%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombophlebitis			
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Venous thrombosis			
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Venous thrombosis limb			
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	2 / 452 (0.44%)	4 / 461 (0.87%)	
occurrences causally related to treatment / all	0 / 2	1 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Catheter site discharge			

subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest pain			
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (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	2 / 452 (0.44%)	0 / 461 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gait disturbance			
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General physical health deterioration			
subjects affected / exposed	3 / 452 (0.66%)	9 / 461 (1.95%)	
occurrences causally related to treatment / all	1 / 3	1 / 10	
deaths causally related to treatment / all	0 / 0	0 / 3	
Generalised oedema			
subjects affected / exposed	0 / 452 (0.00%)	6 / 461 (1.30%)	
occurrences causally related to treatment / all	0 / 0	10 / 10	
deaths causally related to treatment / all	0 / 0	1 / 1	
Hernia pain			
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)	
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	0 / 452 (0.00%)	5 / 461 (1.08%)	
occurrences causally related to treatment / all	0 / 0	4 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malaise			

subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple organ dysfunction syndrome			
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Non-cardiac chest pain			
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	6 / 452 (1.33%)	3 / 461 (0.65%)	
occurrences causally related to treatment / all	0 / 7	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	1 / 452 (0.22%)	1 / 461 (0.22%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Female genital tract fistula			
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine haemorrhage			
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vaginal haemorrhage			
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Respiratory, thoracic and mediastinal disorders			
Bronchitis chronic			
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			
subjects affected / exposed	6 / 452 (1.33%)	4 / 461 (0.87%)	
occurrences causally related to treatment / all	3 / 8	1 / 4	
deaths causally related to treatment / all	1 / 1	0 / 0	
Dyspnoea exertional			
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hydrothorax			
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung infiltration			
subjects affected / exposed	1 / 452 (0.22%)	1 / 461 (0.22%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			
subjects affected / exposed	7 / 452 (1.55%)	14 / 461 (3.04%)	
occurrences causally related to treatment / all	5 / 11	15 / 23	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumothorax			
subjects affected / exposed	2 / 452 (0.44%)	1 / 461 (0.22%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Pulmonary artery thrombosis subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism subjects affected / exposed	8 / 452 (1.77%)	4 / 461 (0.87%)	
occurrences causally related to treatment / all	5 / 8	1 / 4	
deaths causally related to treatment / all	0 / 0	0 / 1	
Respiratory failure subjects affected / exposed	0 / 452 (0.00%)	2 / 461 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Depression subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Depressive symptom subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Somatic symptom disorder subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)	
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	0 / 452 (0.00%)	1 / 461 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Alanine aminotransferase abnormal subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Alanine aminotransferase increased			
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aspartate aminotransferase abnormal			
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood bilirubin abnormal			
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood glucose increased			
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General physical condition abnormal			
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic enzyme increased			
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nutritional condition abnormal			
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Platelet count decreased			

subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Weight increased			
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Femur fracture			
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hip fracture			
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Humerus fracture			
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Incisional hernia			
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lumbar vertebral fracture			
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Patella fracture			
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Procedural haemorrhage			

subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal fracture			
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Cardiac arrest			
subjects affected / exposed	1 / 452 (0.22%)	1 / 461 (0.22%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	1 / 1	0 / 1	
Cardiac failure			
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardio-respiratory arrest			
subjects affected / exposed	1 / 452 (0.22%)	1 / 461 (0.22%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Cardiomyopathy			
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiopulmonary failure			
subjects affected / exposed	0 / 452 (0.00%)	2 / 461 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 2	
Myocardial infarction			
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinus tachycardia			

subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tachycardia			
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Cerebral haemorrhage			
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral ischaemia			
subjects affected / exposed	2 / 452 (0.44%)	0 / 461 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral venous thrombosis			
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrovascular accident			
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (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	1 / 452 (0.22%)	0 / 461 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Headache			
subjects affected / exposed	2 / 452 (0.44%)	2 / 461 (0.43%)	
occurrences causally related to treatment / all	1 / 2	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Loss of consciousness			

subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Paraesthesia			
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Radiculopathy			
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seizure			
subjects affected / exposed	0 / 452 (0.00%)	2 / 461 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (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	4 / 452 (0.88%)	1 / 461 (0.22%)	
occurrences causally related to treatment / all	3 / 6	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile neutropenia			
subjects affected / exposed	2 / 452 (0.44%)	0 / 461 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenia			
subjects affected / exposed	3 / 452 (0.66%)	2 / 461 (0.43%)	
occurrences causally related to treatment / all	1 / 3	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancytopenia			

subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (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	2 / 452 (0.44%)	2 / 461 (0.43%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Visual impairment			
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	0 / 452 (0.00%)	3 / 461 (0.65%)	
occurrences causally related to treatment / all	0 / 0	1 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain			
subjects affected / exposed	11 / 452 (2.43%)	10 / 461 (2.17%)	
occurrences causally related to treatment / all	2 / 11	2 / 11	
deaths causally related to treatment / all	0 / 0	1 / 1	
Abdominal pain upper			
subjects affected / exposed	3 / 452 (0.66%)	1 / 461 (0.22%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal wall disorder			
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (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	3 / 452 (0.66%)	13 / 461 (2.82%)	
occurrences causally related to treatment / all	1 / 3	4 / 13	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis			

subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Constipation			
subjects affected / exposed	1 / 452 (0.22%)	4 / 461 (0.87%)	
occurrences causally related to treatment / all	0 / 1	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	4 / 452 (0.88%)	2 / 461 (0.43%)	
occurrences causally related to treatment / all	2 / 4	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysphagia			
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric perforation			
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal obstruction			
subjects affected / exposed	1 / 452 (0.22%)	1 / 461 (0.22%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhagic ascites			
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileus			

subjects affected / exposed	7 / 452 (1.55%)	10 / 461 (2.17%)	
occurrences causally related to treatment / all	1 / 11	6 / 10	
deaths causally related to treatment / all	0 / 1	0 / 0	
Ileus paralytic			
subjects affected / exposed	2 / 452 (0.44%)	1 / 461 (0.22%)	
occurrences causally related to treatment / all	2 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal fistula			
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal obstruction			
subjects affected / exposed	20 / 452 (4.42%)	23 / 461 (4.99%)	
occurrences causally related to treatment / all	1 / 23	5 / 31	
deaths causally related to treatment / all	0 / 2	0 / 1	
Intestinal perforation			
subjects affected / exposed	0 / 452 (0.00%)	2 / 461 (0.43%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Jejunal stenosis			
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (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	1 / 452 (0.22%)	1 / 461 (0.22%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Large intestine perforation			
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Melaena			

subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mesenteric artery thrombosis			
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mesenteric vascular occlusion			
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Nausea			
subjects affected / exposed	4 / 452 (0.88%)	7 / 461 (1.52%)	
occurrences causally related to treatment / all	0 / 4	2 / 9	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal ulcer			
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophagitis			
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis acute			
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal haemorrhage			
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal stenosis			

subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (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	7 / 452 (1.55%)	11 / 461 (2.39%)	
occurrences causally related to treatment / all	0 / 9	0 / 15	
deaths causally related to treatment / all	0 / 0	0 / 1	
Small intestinal perforation			
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subileus			
subjects affected / exposed	11 / 452 (2.43%)	9 / 461 (1.95%)	
occurrences causally related to treatment / all	0 / 12	0 / 11	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	8 / 452 (1.77%)	7 / 461 (1.52%)	
occurrences causally related to treatment / all	0 / 9	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Bile duct obstruction			
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis acute			
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic failure			
subjects affected / exposed	0 / 452 (0.00%)	2 / 461 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			

Drug eruption			
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin ulcer			
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	2 / 452 (0.44%)	1 / 461 (0.22%)	
occurrences causally related to treatment / all	1 / 2	2 / 2	
deaths causally related to treatment / all	0 / 0	1 / 1	
Bladder disorder			
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hydronephrosis			
subjects affected / exposed	2 / 452 (0.44%)	2 / 461 (0.43%)	
occurrences causally related to treatment / all	1 / 2	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oliguria			
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelocaliectasis			
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal colic			
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal failure			

subjects affected / exposed	1 / 452 (0.22%)	1 / 461 (0.22%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 1	
Ureteric obstruction			
subjects affected / exposed	1 / 452 (0.22%)	1 / 461 (0.22%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urethral disorder			
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary retention			
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (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	1 / 452 (0.22%)	2 / 461 (0.43%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Flank pain			
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoarthritis			
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Scleroderma			
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			

Acute sinusitis			
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis			
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacteraemia			
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacterial infection			
subjects affected / exposed	1 / 452 (0.22%)	1 / 461 (0.22%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacterial pyelonephritis			
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Candida infection			
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Catheter site infection			
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	0 / 452 (0.00%)	2 / 461 (0.43%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cystitis			

subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (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	1 / 452 (0.22%)	2 / 461 (0.43%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enteritis infectious			
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterocolitis infectious			
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Erysipelas			
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia bacteraemia			
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile infection			
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastritis viral			
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			

subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes zoster			
subjects affected / exposed	2 / 452 (0.44%)	0 / 461 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Incision site infection			
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infected skin ulcer			
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infection			
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Klebsiella infection			
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Legionella infection			
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung infection			

subjects affected / exposed	0 / 452 (0.00%)	2 / 461 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenic sepsis			
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritonitis			
subjects affected / exposed	0 / 452 (0.00%)	3 / 461 (0.65%)	
occurrences causally related to treatment / all	0 / 0	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	4 / 452 (0.88%)	4 / 461 (0.87%)	
occurrences causally related to treatment / all	2 / 10	0 / 4	
deaths causally related to treatment / all	1 / 1	0 / 0	
Pneumonia bacterial			
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (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	0 / 452 (0.00%)	1 / 461 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory tract infection			
subjects affected / exposed	3 / 452 (0.66%)	2 / 461 (0.43%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic shock			

subjects affected / exposed	1 / 452 (0.22%)	1 / 461 (0.22%)	
occurrences causally related to treatment / all	0 / 1	2 / 2	
deaths causally related to treatment / all	0 / 0	1 / 1	
Skin infection			
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal sepsis			
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	2 / 452 (0.44%)	3 / 461 (0.65%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urosepsis			
subjects affected / exposed	1 / 452 (0.22%)	1 / 461 (0.22%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound sepsis			
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 452 (0.00%)	2 / 461 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dehydration			
subjects affected / exposed	4 / 452 (0.88%)	4 / 461 (0.87%)	
occurrences causally related to treatment / all	1 / 4	2 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic ketoacidosis			

subjects affected / exposed	0 / 452 (0.00%)	2 / 461 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Failure to thrive			
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperkalaemia			
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoalbuminaemia			
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypokalaemia			
subjects affected / exposed	1 / 452 (0.22%)	3 / 461 (0.65%)	
occurrences causally related to treatment / all	0 / 2	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyponatraemia			
subjects affected / exposed	1 / 452 (0.22%)	1 / 461 (0.22%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypophosphataemia			
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)	
occurrences causally related to treatment / all	0 / 1	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	Placebo + Paclitaxel	Trebananib + Paclitaxel	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	434 / 452 (96.02%)	443 / 461 (96.10%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute myeloid leukaemia			
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)	
occurrences (all)	0	1	
Basal cell carcinoma			
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)	
occurrences (all)	0	1	
Cancer pain			
subjects affected / exposed	0 / 452 (0.00%)	2 / 461 (0.43%)	
occurrences (all)	0	4	
Malignant ascites			
subjects affected / exposed	1 / 452 (0.22%)	1 / 461 (0.22%)	
occurrences (all)	2	1	
Malignant pleural effusion			
subjects affected / exposed	0 / 452 (0.00%)	2 / 461 (0.43%)	
occurrences (all)	0	3	
Pelvic neoplasm			
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)	
occurrences (all)	0	1	
Squamous cell carcinoma of skin			
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)	
occurrences (all)	1	0	
Tumour pain			
subjects affected / exposed	1 / 452 (0.22%)	2 / 461 (0.43%)	
occurrences (all)	2	2	
Vaginal neoplasm			
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)	
occurrences (all)	0	1	
Vascular disorders			
Angiopathy			
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)	
occurrences (all)	1	0	
Arteriosclerosis			

subjects affected / exposed	1 / 452 (0.22%)	1 / 461 (0.22%)
occurrences (all)	1	2
Blood pressure fluctuation		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Capillary disorder		
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)
occurrences (all)	1	0
Deep vein thrombosis		
subjects affected / exposed	4 / 452 (0.88%)	9 / 461 (1.95%)
occurrences (all)	4	12
Erythromelalgia		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	7
Flushing		
subjects affected / exposed	18 / 452 (3.98%)	23 / 461 (4.99%)
occurrences (all)	26	31
Haematoma		
subjects affected / exposed	10 / 452 (2.21%)	7 / 461 (1.52%)
occurrences (all)	10	9
Haemodynamic instability		
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)
occurrences (all)	1	0
Haemorrhage		
subjects affected / exposed	1 / 452 (0.22%)	1 / 461 (0.22%)
occurrences (all)	2	1
Hot flush		
subjects affected / exposed	19 / 452 (4.20%)	17 / 461 (3.69%)
occurrences (all)	23	21
Hyperaemia		
subjects affected / exposed	0 / 452 (0.00%)	2 / 461 (0.43%)
occurrences (all)	0	5
Hypertension		
subjects affected / exposed	18 / 452 (3.98%)	30 / 461 (6.51%)
occurrences (all)	23	39
Hypertensive crisis		

subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	2
Hypotension		
subjects affected / exposed	11 / 452 (2.43%)	14 / 461 (3.04%)
occurrences (all)	13	14
Iliac vein occlusion		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Inferior vena caval occlusion		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Ischaemia		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Jugular vein thrombosis		
subjects affected / exposed	1 / 452 (0.22%)	1 / 461 (0.22%)
occurrences (all)	1	1
Labile blood pressure		
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)
occurrences (all)	1	0
Lymphoedema		
subjects affected / exposed	8 / 452 (1.77%)	30 / 461 (6.51%)
occurrences (all)	14	66
Lymphorrhoea		
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)
occurrences (all)	1	0
Orthostatic hypotension		
subjects affected / exposed	1 / 452 (0.22%)	5 / 461 (1.08%)
occurrences (all)	1	5
Pallor		
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)
occurrences (all)	1	0
Peripheral coldness		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Peripheral venous disease		

subjects affected / exposed	2 / 452 (0.44%)	0 / 461 (0.00%)	
occurrences (all)	2	0	
Phlebitis			
subjects affected / exposed	0 / 452 (0.00%)	5 / 461 (1.08%)	
occurrences (all)	0	5	
Post thrombotic syndrome			
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)	
occurrences (all)	0	1	
Raynaud's phenomenon			
subjects affected / exposed	1 / 452 (0.22%)	2 / 461 (0.43%)	
occurrences (all)	1	2	
Thrombophlebitis			
subjects affected / exposed	1 / 452 (0.22%)	3 / 461 (0.65%)	
occurrences (all)	2	5	
Thrombophlebitis superficial			
subjects affected / exposed	1 / 452 (0.22%)	2 / 461 (0.43%)	
occurrences (all)	1	2	
Thrombosis			
subjects affected / exposed	1 / 452 (0.22%)	1 / 461 (0.22%)	
occurrences (all)	1	2	
Varicose vein			
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)	
occurrences (all)	3	0	
Vascular pain			
subjects affected / exposed	1 / 452 (0.22%)	1 / 461 (0.22%)	
occurrences (all)	1	1	
Vasculitis			
subjects affected / exposed	2 / 452 (0.44%)	1 / 461 (0.22%)	
occurrences (all)	2	1	
Venous thrombosis limb			
subjects affected / exposed	2 / 452 (0.44%)	3 / 461 (0.65%)	
occurrences (all)	2	3	
Venous thrombosis			
subjects affected / exposed	3 / 452 (0.66%)	3 / 461 (0.65%)	
occurrences (all)	3	3	
Surgical and medical procedures			

Asthma prophylaxis			
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)	
occurrences (all)	1	0	
Chemotherapy neurotoxicity attenuation			
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)	
occurrences (all)	0	1	
Endodontic procedure			
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)	
occurrences (all)	0	1	
Papilloma excision			
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)	
occurrences (all)	1	0	
Wound drainage			
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
Administration site pain			
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)	
occurrences (all)	0	1	
Adverse drug reaction			
subjects affected / exposed	2 / 452 (0.44%)	2 / 461 (0.43%)	
occurrences (all)	2	2	
Asthenia			
subjects affected / exposed	120 / 452 (26.55%)	130 / 461 (28.20%)	
occurrences (all)	257	321	
Axillary pain			
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)	
occurrences (all)	0	1	
Catheter site bruise			
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)	
occurrences (all)	0	1	
Catheter site discharge			
subjects affected / exposed	1 / 452 (0.22%)	1 / 461 (0.22%)	
occurrences (all)	1	1	
Catheter site erythema			

subjects affected / exposed	0 / 452 (0.00%)	2 / 461 (0.43%)
occurrences (all)	0	3
Catheter site haematoma		
subjects affected / exposed	0 / 452 (0.00%)	2 / 461 (0.43%)
occurrences (all)	0	2
Catheter site oedema		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Catheter site pain		
subjects affected / exposed	10 / 452 (2.21%)	13 / 461 (2.82%)
occurrences (all)	10	13
Catheter site rash		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Catheter site related reaction		
subjects affected / exposed	1 / 452 (0.22%)	1 / 461 (0.22%)
occurrences (all)	1	1
Catheter site swelling		
subjects affected / exposed	0 / 452 (0.00%)	2 / 461 (0.43%)
occurrences (all)	0	3
Chest discomfort		
subjects affected / exposed	3 / 452 (0.66%)	3 / 461 (0.65%)
occurrences (all)	3	5
Chest pain		
subjects affected / exposed	16 / 452 (3.54%)	20 / 461 (4.34%)
occurrences (all)	20	25
Chills		
subjects affected / exposed	13 / 452 (2.88%)	8 / 461 (1.74%)
occurrences (all)	19	11
Complication associated with device		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Crepitations		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Discomfort		

subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)
occurrences (all)	4	0
Drug intolerance		
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)
occurrences (all)	1	0
Early satiety		
subjects affected / exposed	3 / 452 (0.66%)	4 / 461 (0.87%)
occurrences (all)	6	7
Extravasation		
subjects affected / exposed	1 / 452 (0.22%)	3 / 461 (0.65%)
occurrences (all)	1	3
Facial pain		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	3
Fatigue		
subjects affected / exposed	137 / 452 (30.31%)	128 / 461 (27.77%)
occurrences (all)	304	302
Feeling abnormal		
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)
occurrences (all)	1	0
Feeling cold		
subjects affected / exposed	1 / 452 (0.22%)	2 / 461 (0.43%)
occurrences (all)	1	2
Feeling hot		
subjects affected / exposed	2 / 452 (0.44%)	3 / 461 (0.65%)
occurrences (all)	2	24
Feeling jittery		
subjects affected / exposed	0 / 452 (0.00%)	2 / 461 (0.43%)
occurrences (all)	0	2
Gait disturbance		
subjects affected / exposed	1 / 452 (0.22%)	3 / 461 (0.65%)
occurrences (all)	1	4
General physical health deterioration		
subjects affected / exposed	4 / 452 (0.88%)	6 / 461 (1.30%)
occurrences (all)	6	8
Generalised oedema		

subjects affected / exposed	12 / 452 (2.65%)	53 / 461 (11.50%)
occurrences (all)	18	97
Hyperthermia		
subjects affected / exposed	1 / 452 (0.22%)	2 / 461 (0.43%)
occurrences (all)	1	3
Hypothermia		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Impaired healing		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Inflammation		
subjects affected / exposed	3 / 452 (0.66%)	1 / 461 (0.22%)
occurrences (all)	3	1
Influenza like illness		
subjects affected / exposed	16 / 452 (3.54%)	12 / 461 (2.60%)
occurrences (all)	28	16
Infusion site extravasation		
subjects affected / exposed	0 / 452 (0.00%)	2 / 461 (0.43%)
occurrences (all)	0	3
Infusion site pruritus		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Infusion site swelling		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Injection site bruising		
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)
occurrences (all)	1	0
Injection site erythema		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Injection site haemorrhage		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Injection site pain		

subjects affected / exposed	3 / 452 (0.66%)	0 / 461 (0.00%)
occurrences (all)	4	0
Injection site pruritus		
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)
occurrences (all)	1	0
Injection site rash		
subjects affected / exposed	2 / 452 (0.44%)	0 / 461 (0.00%)
occurrences (all)	2	0
Injection site reaction		
subjects affected / exposed	1 / 452 (0.22%)	1 / 461 (0.22%)
occurrences (all)	1	1
Local swelling		
subjects affected / exposed	0 / 452 (0.00%)	2 / 461 (0.43%)
occurrences (all)	0	2
Localised oedema		
subjects affected / exposed	122 / 452 (26.99%)	271 / 461 (58.79%)
occurrences (all)	226	724
Malaise		
subjects affected / exposed	6 / 452 (1.33%)	7 / 461 (1.52%)
occurrences (all)	9	7
Mass		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Medical device pain		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Mucosal dryness		
subjects affected / exposed	2 / 452 (0.44%)	1 / 461 (0.22%)
occurrences (all)	2	1
Mucosal inflammation		
subjects affected / exposed	34 / 452 (7.52%)	22 / 461 (4.77%)
occurrences (all)	49	32
Nodule		
subjects affected / exposed	1 / 452 (0.22%)	3 / 461 (0.65%)
occurrences (all)	1	3
Non-cardiac chest pain		

subjects affected / exposed	3 / 452 (0.66%)	5 / 461 (1.08%)
occurrences (all)	3	5
Pain		
subjects affected / exposed	19 / 452 (4.20%)	24 / 461 (5.21%)
occurrences (all)	21	27
Performance status decreased		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Peripheral swelling		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Polyp		
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)
occurrences (all)	1	0
Puncture site discharge		
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)
occurrences (all)	1	0
Pyrexia		
subjects affected / exposed	62 / 452 (13.72%)	41 / 461 (8.89%)
occurrences (all)	79	54
Secretion discharge		
subjects affected / exposed	1 / 452 (0.22%)	1 / 461 (0.22%)
occurrences (all)	1	1
Sensation of foreign body		
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)
occurrences (all)	1	0
Suprapubic pain		
subjects affected / exposed	0 / 452 (0.00%)	2 / 461 (0.43%)
occurrences (all)	0	3
Temperature intolerance		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	2
Ulcer		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Xerosis		

subjects affected / exposed occurrences (all)	1 / 452 (0.22%) 1	0 / 461 (0.00%) 0	
Immune system disorders			
Allergy to arthropod sting			
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)	
occurrences (all)	1	0	
Contrast media allergy			
subjects affected / exposed	3 / 452 (0.66%)	2 / 461 (0.43%)	
occurrences (all)	3	2	
Drug hypersensitivity			
subjects affected / exposed	3 / 452 (0.66%)	4 / 461 (0.87%)	
occurrences (all)	4	5	
Food allergy			
subjects affected / exposed	0 / 452 (0.00%)	2 / 461 (0.43%)	
occurrences (all)	0	2	
Hypersensitivity			
subjects affected / exposed	12 / 452 (2.65%)	12 / 461 (2.60%)	
occurrences (all)	14	14	
Iodine allergy			
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)	
occurrences (all)	0	1	
Multiple allergies			
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)	
occurrences (all)	0	1	
Seasonal allergy			
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)	
occurrences (all)	0	1	
Reproductive system and breast disorders			
Breast discharge			
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)	
occurrences (all)	0	1	
Breast discomfort			
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)	
occurrences (all)	1	0	
Breast pain			

subjects affected / exposed	8 / 452 (1.77%)	2 / 461 (0.43%)
occurrences (all)	8	3
Breast inflammation		
subjects affected / exposed	2 / 452 (0.44%)	1 / 461 (0.22%)
occurrences (all)	2	1
Erectile dysfunction		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Female genital tract fistula		
subjects affected / exposed	1 / 452 (0.22%)	1 / 461 (0.22%)
occurrences (all)	3	1
Genital haemorrhage		
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)
occurrences (all)	3	0
Genital rash		
subjects affected / exposed	1 / 452 (0.22%)	1 / 461 (0.22%)
occurrences (all)	1	1
Genital lesion		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Metrorrhagia		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Pelvic discomfort		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Pelvic pain		
subjects affected / exposed	6 / 452 (1.33%)	8 / 461 (1.74%)
occurrences (all)	8	13
Perineal erythema		
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)
occurrences (all)	1	0
Pruritus genital		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Uterine cervix stenosis		

subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)	
occurrences (all)	0	1	
Vaginal discharge			
subjects affected / exposed	4 / 452 (0.88%)	7 / 461 (1.52%)	
occurrences (all)	4	8	
Vaginal haemorrhage			
subjects affected / exposed	8 / 452 (1.77%)	3 / 461 (0.65%)	
occurrences (all)	12	3	
Vaginal inflammation			
subjects affected / exposed	1 / 452 (0.22%)	1 / 461 (0.22%)	
occurrences (all)	1	1	
Vulval ulceration			
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)	
occurrences (all)	2	0	
Vulvovaginal burning sensation			
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)	
occurrences (all)	2	0	
Vulvovaginal discomfort			
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)	
occurrences (all)	0	1	
Vulvovaginal pain			
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)	
occurrences (all)	0	1	
Vulvovaginal dryness			
subjects affected / exposed	1 / 452 (0.22%)	3 / 461 (0.65%)	
occurrences (all)	1	3	
Vulvovaginal pruritus			
subjects affected / exposed	2 / 452 (0.44%)	2 / 461 (0.43%)	
occurrences (all)	2	2	
Vulvovaginal swelling			
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Acquired diaphragmatic eventration			

subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)
occurrences (all)	1	0
Allergic cough		
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)
occurrences (all)	1	0
Asthma		
subjects affected / exposed	2 / 452 (0.44%)	1 / 461 (0.22%)
occurrences (all)	4	1
Atelectasis		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Bradypnoea		
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)
occurrences (all)	1	0
Bronchial obstruction		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Bronchiectasis		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Bronchospasm		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Catarrh		
subjects affected / exposed	3 / 452 (0.66%)	3 / 461 (0.65%)
occurrences (all)	3	4
Chylothorax		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Cough		
subjects affected / exposed	62 / 452 (13.72%)	72 / 461 (15.62%)
occurrences (all)	83	115
Cough decreased		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Dry throat		

subjects affected / exposed	1 / 452 (0.22%)	1 / 461 (0.22%)
occurrences (all)	1	1
Dysphonia		
subjects affected / exposed	6 / 452 (1.33%)	13 / 461 (2.82%)
occurrences (all)	8	13
Dyspnoea		
subjects affected / exposed	55 / 452 (12.17%)	74 / 461 (16.05%)
occurrences (all)	80	137
Dyspnoea exertional		
subjects affected / exposed	11 / 452 (2.43%)	22 / 461 (4.77%)
occurrences (all)	11	32
Epistaxis		
subjects affected / exposed	35 / 452 (7.74%)	23 / 461 (4.99%)
occurrences (all)	42	31
Hiccups		
subjects affected / exposed	1 / 452 (0.22%)	1 / 461 (0.22%)
occurrences (all)	2	1
Hydrothorax		
subjects affected / exposed	1 / 452 (0.22%)	3 / 461 (0.65%)
occurrences (all)	1	3
Hyperventilation		
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)
occurrences (all)	6	0
Hypoventilation		
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)
occurrences (all)	1	0
Hypoxia		
subjects affected / exposed	1 / 452 (0.22%)	1 / 461 (0.22%)
occurrences (all)	1	3
Increased bronchial secretion		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Interstitial lung disease		
subjects affected / exposed	2 / 452 (0.44%)	1 / 461 (0.22%)
occurrences (all)	2	1
Laryngeal discomfort		

subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)
occurrences (all)	1	0
Lung infiltration		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Middle lobe syndrome		
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)
occurrences (all)	1	0
Nasal congestion		
subjects affected / exposed	10 / 452 (2.21%)	10 / 461 (2.17%)
occurrences (all)	12	13
Nasal discomfort		
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)
occurrences (all)	1	0
Nasal disorder		
subjects affected / exposed	1 / 452 (0.22%)	1 / 461 (0.22%)
occurrences (all)	1	1
Nasal dryness		
subjects affected / exposed	1 / 452 (0.22%)	1 / 461 (0.22%)
occurrences (all)	1	1
Oropharyngeal pain		
subjects affected / exposed	20 / 452 (4.42%)	18 / 461 (3.90%)
occurrences (all)	26	22
Orthopnoea		
subjects affected / exposed	1 / 452 (0.22%)	2 / 461 (0.43%)
occurrences (all)	1	2
Painful respiration		
subjects affected / exposed	0 / 452 (0.00%)	2 / 461 (0.43%)
occurrences (all)	0	2
Pharyngeal erythema		
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)
occurrences (all)	1	0
Pharyngeal inflammation		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Pleural effusion		

subjects affected / exposed	13 / 452 (2.88%)	62 / 461 (13.45%)
occurrences (all)	16	79
Pleural thickening		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Pleurisy		
subjects affected / exposed	1 / 452 (0.22%)	3 / 461 (0.65%)
occurrences (all)	1	3
Pneumonitis		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Pneumothorax		
subjects affected / exposed	1 / 452 (0.22%)	1 / 461 (0.22%)
occurrences (all)	1	1
Productive cough		
subjects affected / exposed	10 / 452 (2.21%)	11 / 461 (2.39%)
occurrences (all)	13	13
Pulmonary embolism		
subjects affected / exposed	3 / 452 (0.66%)	1 / 461 (0.22%)
occurrences (all)	3	2
Pulmonary arterial hypertension		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Pulmonary fibrosis		
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)
occurrences (all)	1	0
Rales		
subjects affected / exposed	1 / 452 (0.22%)	1 / 461 (0.22%)
occurrences (all)	1	1
Respiratory disorder		
subjects affected / exposed	1 / 452 (0.22%)	1 / 461 (0.22%)
occurrences (all)	1	1
Respiratory tract congestion		
subjects affected / exposed	2 / 452 (0.44%)	1 / 461 (0.22%)
occurrences (all)	3	2
Rhinitis allergic		

subjects affected / exposed	8 / 452 (1.77%)	6 / 461 (1.30%)	
occurrences (all)	9	6	
Rhinorrhoea			
subjects affected / exposed	8 / 452 (1.77%)	18 / 461 (3.90%)	
occurrences (all)	8	23	
Sinus congestion			
subjects affected / exposed	1 / 452 (0.22%)	4 / 461 (0.87%)	
occurrences (all)	1	4	
Sinus pain			
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)	
occurrences (all)	0	1	
Sneezing			
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)	
occurrences (all)	1	0	
Throat irritation			
subjects affected / exposed	1 / 452 (0.22%)	2 / 461 (0.43%)	
occurrences (all)	1	2	
Sputum discoloured			
subjects affected / exposed	0 / 452 (0.00%)	2 / 461 (0.43%)	
occurrences (all)	0	2	
Throat tightness			
subjects affected / exposed	1 / 452 (0.22%)	1 / 461 (0.22%)	
occurrences (all)	1	1	
Tracheal inflammation			
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)	
occurrences (all)	1	0	
Upper respiratory tract inflammation			
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)	
occurrences (all)	1	0	
Upper-airway cough syndrome			
subjects affected / exposed	0 / 452 (0.00%)	2 / 461 (0.43%)	
occurrences (all)	0	3	
Wheezing			
subjects affected / exposed	0 / 452 (0.00%)	2 / 461 (0.43%)	
occurrences (all)	0	2	
Psychiatric disorders			

Adjustment disorder		
subjects affected / exposed	0 / 452 (0.00%)	2 / 461 (0.43%)
occurrences (all)	0	2
Agitation		
subjects affected / exposed	2 / 452 (0.44%)	4 / 461 (0.87%)
occurrences (all)	2	6
Affect lability		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Alcohol withdrawal syndrome		
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)
occurrences (all)	1	0
Anxiety		
subjects affected / exposed	35 / 452 (7.74%)	32 / 461 (6.94%)
occurrences (all)	38	35
Anxiety disorder due to a general medical condition		
subjects affected / exposed	2 / 452 (0.44%)	0 / 461 (0.00%)
occurrences (all)	2	0
Bradyphrenia		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	2
Confusional state		
subjects affected / exposed	0 / 452 (0.00%)	3 / 461 (0.65%)
occurrences (all)	0	3
Delirium		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Depressed mood		
subjects affected / exposed	2 / 452 (0.44%)	1 / 461 (0.22%)
occurrences (all)	3	1
Depression		
subjects affected / exposed	17 / 452 (3.76%)	23 / 461 (4.99%)
occurrences (all)	19	26
Dysphemia		

subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	2
Euphoric mood		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Emotional disorder		
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)
occurrences (all)	2	0
Hallucination		
subjects affected / exposed	0 / 452 (0.00%)	2 / 461 (0.43%)
occurrences (all)	0	2
Insomnia		
subjects affected / exposed	52 / 452 (11.50%)	42 / 461 (9.11%)
occurrences (all)	63	49
Neurosis		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	2
Mood altered		
subjects affected / exposed	7 / 452 (1.55%)	6 / 461 (1.30%)
occurrences (all)	7	7
Restlessness		
subjects affected / exposed	3 / 452 (0.66%)	2 / 461 (0.43%)
occurrences (all)	3	4
Sleep disorder		
subjects affected / exposed	1 / 452 (0.22%)	1 / 461 (0.22%)
occurrences (all)	1	1
Somatic symptom disorder		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Stress		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Tic		
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)
occurrences (all)	1	0
Product issues		

Device occlusion subjects affected / exposed occurrences (all)	0 / 452 (0.00%) 0	1 / 461 (0.22%) 1	
Thrombosis in device subjects affected / exposed occurrences (all)	1 / 452 (0.22%) 1	1 / 461 (0.22%) 1	
Hepatobiliary disorders			
Cholecystitis chronic subjects affected / exposed occurrences (all)	1 / 452 (0.22%) 1	0 / 461 (0.00%) 0	
Cholestasis subjects affected / exposed occurrences (all)	0 / 452 (0.00%) 0	1 / 461 (0.22%) 4	
Gallbladder pain subjects affected / exposed occurrences (all)	0 / 452 (0.00%) 0	2 / 461 (0.43%) 2	
Hepatic function abnormal subjects affected / exposed occurrences (all)	1 / 452 (0.22%) 2	0 / 461 (0.00%) 0	
Hepatic pain subjects affected / exposed occurrences (all)	0 / 452 (0.00%) 0	2 / 461 (0.43%) 2	
Hepatitis subjects affected / exposed occurrences (all)	0 / 452 (0.00%) 0	1 / 461 (0.22%) 1	
Hepatotoxicity subjects affected / exposed occurrences (all)	1 / 452 (0.22%) 2	1 / 461 (0.22%) 1	
Hyperbilirubinaemia subjects affected / exposed occurrences (all)	2 / 452 (0.44%) 2	1 / 461 (0.22%) 1	
Jaundice subjects affected / exposed occurrences (all)	1 / 452 (0.22%) 1	1 / 461 (0.22%) 1	
Portal vein thrombosis			

subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)	
occurrences (all)	0	1	
Investigations			
Alanine aminotransferase abnormal			
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)	
occurrences (all)	2	0	
Alanine aminotransferase increased			
subjects affected / exposed	5 / 452 (1.11%)	5 / 461 (1.08%)	
occurrences (all)	9	8	
Aspartate aminotransferase abnormal			
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)	
occurrences (all)	2	0	
Aspartate aminotransferase increased			
subjects affected / exposed	5 / 452 (1.11%)	3 / 461 (0.65%)	
occurrences (all)	8	4	
Biopsy breast abnormal			
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)	
occurrences (all)	0	1	
Blood albumin decreased			
subjects affected / exposed	1 / 452 (0.22%)	2 / 461 (0.43%)	
occurrences (all)	2	3	
Blood alkaline phosphatase abnormal			
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)	
occurrences (all)	0	1	
Blood alkaline phosphatase increased			
subjects affected / exposed	4 / 452 (0.88%)	6 / 461 (1.30%)	
occurrences (all)	4	9	
Blood bicarbonate decreased			
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)	
occurrences (all)	0	1	
Blood bilirubin abnormal			
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)	
occurrences (all)	1	0	
Blood bilirubin increased			

subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Blood calcium decreased		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Blood calcium increased		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Blood cholesterol increased		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Blood creatine increased		
subjects affected / exposed	2 / 452 (0.44%)	1 / 461 (0.22%)
occurrences (all)	2	1
Blood creatinine		
subjects affected / exposed	1 / 452 (0.22%)	1 / 461 (0.22%)
occurrences (all)	1	1
Blood creatinine increased		
subjects affected / exposed	3 / 452 (0.66%)	11 / 461 (2.39%)
occurrences (all)	6	18
Blood electrolytes decreased		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	2
Blood glucose increased		
subjects affected / exposed	1 / 452 (0.22%)	1 / 461 (0.22%)
occurrences (all)	1	1
Blood lactate dehydrogenase increased		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Blood magnesium decreased		
subjects affected / exposed	3 / 452 (0.66%)	2 / 461 (0.43%)
occurrences (all)	4	3
Blood phosphorus decreased		
subjects affected / exposed	2 / 452 (0.44%)	0 / 461 (0.00%)
occurrences (all)	2	0

Blood potassium decreased subjects affected / exposed occurrences (all)	1 / 452 (0.22%) 1	1 / 461 (0.22%) 2
Blood potassium increased subjects affected / exposed occurrences (all)	1 / 452 (0.22%) 1	2 / 461 (0.43%) 2
Blood sodium decreased subjects affected / exposed occurrences (all)	1 / 452 (0.22%) 1	1 / 461 (0.22%) 1
Blood triglycerides increased subjects affected / exposed occurrences (all)	1 / 452 (0.22%) 2	1 / 461 (0.22%) 1
Blood urea increased subjects affected / exposed occurrences (all)	2 / 452 (0.44%) 2	2 / 461 (0.43%) 3
Breath sounds abnormal subjects affected / exposed occurrences (all)	1 / 452 (0.22%) 1	1 / 461 (0.22%) 1
Chest x-ray abnormal subjects affected / exposed occurrences (all)	2 / 452 (0.44%) 2	0 / 461 (0.00%) 0
Creatinine renal clearance increased subjects affected / exposed occurrences (all)	1 / 452 (0.22%) 1	0 / 461 (0.00%) 0
Culture urine positive subjects affected / exposed occurrences (all)	0 / 452 (0.00%) 0	1 / 461 (0.22%) 1
Eastern cooperative oncology group performance status worsened subjects affected / exposed occurrences (all)	0 / 452 (0.00%) 0	3 / 461 (0.65%) 4
Electrocardiogram abnormal subjects affected / exposed occurrences (all)	0 / 452 (0.00%) 0	1 / 461 (0.22%) 1
Electrocardiogram change		

subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)
occurrences (all)	1	0
Electrocardiogram qt prolonged		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Gamma-glutamyltransferase abnormal		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Gamma-glutamyltransferase increased		
subjects affected / exposed	2 / 452 (0.44%)	2 / 461 (0.43%)
occurrences (all)	3	4
Glomerular filtration rate decreased		
subjects affected / exposed	1 / 452 (0.22%)	1 / 461 (0.22%)
occurrences (all)	3	2
Glucose tolerance test abnormal		
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)
occurrences (all)	1	0
Haemoglobin		
subjects affected / exposed	3 / 452 (0.66%)	4 / 461 (0.87%)
occurrences (all)	12	6
Haemoglobin abnormal		
subjects affected / exposed	1 / 452 (0.22%)	1 / 461 (0.22%)
occurrences (all)	2	2
Haemoglobin decreased		
subjects affected / exposed	6 / 452 (1.33%)	6 / 461 (1.30%)
occurrences (all)	15	9
International normalised ratio increased		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	2
Lipase increased		
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)
occurrences (all)	1	0
Mammogram normal		

subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Mean cell volume abnormal		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	2
Monocyte count decreased		
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)
occurrences (all)	1	0
Neutrophil count		
subjects affected / exposed	1 / 452 (0.22%)	2 / 461 (0.43%)
occurrences (all)	3	3
Neutrophil count abnormal		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Neutrophil count decreased		
subjects affected / exposed	20 / 452 (4.42%)	14 / 461 (3.04%)
occurrences (all)	92	30
Nutritional condition abnormal		
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)
occurrences (all)	2	0
Oxygen saturation decreased		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Platelet count decreased		
subjects affected / exposed	4 / 452 (0.88%)	1 / 461 (0.22%)
occurrences (all)	6	1
Protein urine		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	2
Protein urine present		
subjects affected / exposed	1 / 452 (0.22%)	1 / 461 (0.22%)
occurrences (all)	1	1
Prothrombin level decreased		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Red blood cells urine		

subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)	
occurrences (all)	0	1	
Red blood cells urine positive			
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)	
occurrences (all)	0	1	
Transaminases increased			
subjects affected / exposed	1 / 452 (0.22%)	2 / 461 (0.43%)	
occurrences (all)	1	2	
Urine output decreased			
subjects affected / exposed	0 / 452 (0.00%)	2 / 461 (0.43%)	
occurrences (all)	0	2	
Urine output increased			
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)	
occurrences (all)	1	0	
Vitamin d decreased			
subjects affected / exposed	1 / 452 (0.22%)	1 / 461 (0.22%)	
occurrences (all)	1	1	
Waist circumference increased			
subjects affected / exposed	0 / 452 (0.00%)	2 / 461 (0.43%)	
occurrences (all)	0	2	
Weight decreased			
subjects affected / exposed	17 / 452 (3.76%)	11 / 461 (2.39%)	
occurrences (all)	34	17	
Weight increased			
subjects affected / exposed	10 / 452 (2.21%)	43 / 461 (9.33%)	
occurrences (all)	25	94	
White blood cell count decreased			
subjects affected / exposed	9 / 452 (1.99%)	5 / 461 (1.08%)	
occurrences (all)	48	26	
Injury, poisoning and procedural complications			
Accidental overdose			
subjects affected / exposed	0 / 452 (0.00%)	2 / 461 (0.43%)	
occurrences (all)	0	3	
Animal bite			

subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Arthropod bite		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Compression fracture		
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)
occurrences (all)	1	0
Contrast media reaction		
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)
occurrences (all)	2	0
Contusion		
subjects affected / exposed	3 / 452 (0.66%)	9 / 461 (1.95%)
occurrences (all)	3	10
Electric shock		
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)
occurrences (all)	1	0
Eye contusion		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Eye injury		
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)
occurrences (all)	1	0
Fall		
subjects affected / exposed	3 / 452 (0.66%)	2 / 461 (0.43%)
occurrences (all)	3	2
Foot fracture		
subjects affected / exposed	0 / 452 (0.00%)	4 / 461 (0.87%)
occurrences (all)	0	5
Fracture		
subjects affected / exposed	1 / 452 (0.22%)	1 / 461 (0.22%)
occurrences (all)	1	1
Gastrointestinal stoma complication		
subjects affected / exposed	0 / 452 (0.00%)	2 / 461 (0.43%)
occurrences (all)	0	2
Haematuria traumatic		

subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)
occurrences (all)	1	0
Head injury		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Incision site complication		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Incisional hernia		
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)
occurrences (all)	1	0
Infusion related reaction		
subjects affected / exposed	2 / 452 (0.44%)	5 / 461 (1.08%)
occurrences (all)	6	5
Joint injury		
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)
occurrences (all)	1	0
Laceration		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Ligament sprain		
subjects affected / exposed	3 / 452 (0.66%)	2 / 461 (0.43%)
occurrences (all)	3	2
Limb crushing injury		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Limb injury		
subjects affected / exposed	3 / 452 (0.66%)	1 / 461 (0.22%)
occurrences (all)	3	1
Lip injury		
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)
occurrences (all)	1	0
Muscle rupture		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Muscle strain		

subjects affected / exposed	1 / 452 (0.22%)	1 / 461 (0.22%)
occurrences (all)	1	1
Neck injury		
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)
occurrences (all)	1	0
Perineal injury		
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)
occurrences (all)	1	0
Procedural nausea		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Procedural pain		
subjects affected / exposed	1 / 452 (0.22%)	5 / 461 (1.08%)
occurrences (all)	1	5
Rib fracture		
subjects affected / exposed	1 / 452 (0.22%)	1 / 461 (0.22%)
occurrences (all)	1	1
Scratch		
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)
occurrences (all)	1	0
Skin abrasion		
subjects affected / exposed	3 / 452 (0.66%)	3 / 461 (0.65%)
occurrences (all)	8	3
Skin wound		
subjects affected / exposed	1 / 452 (0.22%)	1 / 461 (0.22%)
occurrences (all)	1	1
Spinal fracture		
subjects affected / exposed	1 / 452 (0.22%)	1 / 461 (0.22%)
occurrences (all)	1	1
Stoma site pain		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Stoma site reaction		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Sunburn		

subjects affected / exposed	2 / 452 (0.44%)	0 / 461 (0.00%)	
occurrences (all)	2	0	
Thermal burn			
subjects affected / exposed	4 / 452 (0.88%)	1 / 461 (0.22%)	
occurrences (all)	4	2	
Tibia fracture			
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)	
occurrences (all)	0	1	
Tooth fracture			
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)	
occurrences (all)	1	0	
Toxicity to various agents			
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)	
occurrences (all)	1	0	
Vascular access complication			
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)	
occurrences (all)	0	1	
Vascular injury			
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)	
occurrences (all)	1	0	
Wound			
subjects affected / exposed	1 / 452 (0.22%)	1 / 461 (0.22%)	
occurrences (all)	6	1	
Wound complication			
subjects affected / exposed	1 / 452 (0.22%)	1 / 461 (0.22%)	
occurrences (all)	1	1	
Wrist fracture			
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)	
occurrences (all)	0	1	
Congenital, familial and genetic disorders			
Cystic lymphangioma			
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)	
occurrences (all)	1	0	
Gilbert's syndrome			

subjects affected / exposed occurrences (all)	0 / 452 (0.00%) 0	1 / 461 (0.22%) 1	
Pyloric stenosis subjects affected / exposed occurrences (all)	1 / 452 (0.22%) 1	0 / 461 (0.00%) 0	
Thalassaemia beta subjects affected / exposed occurrences (all)	1 / 452 (0.22%) 1	0 / 461 (0.00%) 0	
Cardiac disorders			
Angina pectoris subjects affected / exposed occurrences (all)	3 / 452 (0.66%) 4	1 / 461 (0.22%) 1	
Arrhythmia subjects affected / exposed occurrences (all)	1 / 452 (0.22%) 1	2 / 461 (0.43%) 2	
Arrhythmia supraventricular subjects affected / exposed occurrences (all)	1 / 452 (0.22%) 1	0 / 461 (0.00%) 0	
Atrial fibrillation subjects affected / exposed occurrences (all)	3 / 452 (0.66%) 3	2 / 461 (0.43%) 3	
Atrial tachycardia subjects affected / exposed occurrences (all)	0 / 452 (0.00%) 0	1 / 461 (0.22%) 1	
Atrioventricular block first degree subjects affected / exposed occurrences (all)	1 / 452 (0.22%) 1	0 / 461 (0.00%) 0	
Bundle branch block right subjects affected / exposed occurrences (all)	0 / 452 (0.00%) 0	1 / 461 (0.22%) 1	
Cardiac failure subjects affected / exposed occurrences (all)	1 / 452 (0.22%) 1	0 / 461 (0.00%) 0	
Cardiac failure chronic subjects affected / exposed occurrences (all)	1 / 452 (0.22%) 1	0 / 461 (0.00%) 0	

Cardiomyopathy		
subjects affected / exposed	1 / 452 (0.22%)	1 / 461 (0.22%)
occurrences (all)	1	1
Cyanosis		
subjects affected / exposed	0 / 452 (0.00%)	2 / 461 (0.43%)
occurrences (all)	0	2
Diastolic dysfunction		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Intracardiac thrombus		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Myocardial ischaemia		
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)
occurrences (all)	2	0
Palpitations		
subjects affected / exposed	8 / 452 (1.77%)	7 / 461 (1.52%)
occurrences (all)	10	9
Pericardial effusion		
subjects affected / exposed	3 / 452 (0.66%)	5 / 461 (1.08%)
occurrences (all)	4	5
Right ventricular hypertrophy		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Sinus tachycardia		
subjects affected / exposed	3 / 452 (0.66%)	4 / 461 (0.87%)
occurrences (all)	3	4
Supraventricular extrasystoles		
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)
occurrences (all)	1	0
Tachyarrhythmia		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Tachycardia		
subjects affected / exposed	15 / 452 (3.32%)	16 / 461 (3.47%)
occurrences (all)	17	16

Ventricular extrasystoles subjects affected / exposed occurrences (all)	1 / 452 (0.22%) 1	1 / 461 (0.22%) 1	
Nervous system disorders			
Acute polyneuropathy subjects affected / exposed occurrences (all)	0 / 452 (0.00%) 0	1 / 461 (0.22%) 1	
Amnesia subjects affected / exposed occurrences (all)	1 / 452 (0.22%) 1	0 / 461 (0.00%) 0	
Aphasia subjects affected / exposed occurrences (all)	1 / 452 (0.22%) 1	1 / 461 (0.22%) 1	
Aphonia subjects affected / exposed occurrences (all)	1 / 452 (0.22%) 1	2 / 461 (0.43%) 2	
Balance disorder subjects affected / exposed occurrences (all)	3 / 452 (0.66%) 3	5 / 461 (1.08%) 5	
Burning sensation subjects affected / exposed occurrences (all)	1 / 452 (0.22%) 2	1 / 461 (0.22%) 1	
Carpal tunnel syndrome subjects affected / exposed occurrences (all)	0 / 452 (0.00%) 0	2 / 461 (0.43%) 2	
Cerebrovascular disorder subjects affected / exposed occurrences (all)	1 / 452 (0.22%) 1	0 / 461 (0.00%) 0	
Cervical radiculopathy subjects affected / exposed occurrences (all)	1 / 452 (0.22%) 1	0 / 461 (0.00%) 0	
Cognitive disorder subjects affected / exposed occurrences (all)	1 / 452 (0.22%) 1	2 / 461 (0.43%) 2	
Disturbance in attention			

subjects affected / exposed	2 / 452 (0.44%)	1 / 461 (0.22%)
occurrences (all)	3	1
Dizziness		
subjects affected / exposed	49 / 452 (10.84%)	58 / 461 (12.58%)
occurrences (all)	63	72
Dizziness postural		
subjects affected / exposed	2 / 452 (0.44%)	4 / 461 (0.87%)
occurrences (all)	2	6
Dysaesthesia		
subjects affected / exposed	4 / 452 (0.88%)	3 / 461 (0.65%)
occurrences (all)	7	7
Dysgeusia		
subjects affected / exposed	56 / 452 (12.39%)	40 / 461 (8.68%)
occurrences (all)	90	47
Dyskinesia		
subjects affected / exposed	1 / 452 (0.22%)	2 / 461 (0.43%)
occurrences (all)	1	2
Epilepsy		
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)
occurrences (all)	2	0
Head discomfort		
subjects affected / exposed	1 / 452 (0.22%)	4 / 461 (0.87%)
occurrences (all)	1	5
Headache		
subjects affected / exposed	78 / 452 (17.26%)	65 / 461 (14.10%)
occurrences (all)	126	102
Hyperaesthesia		
subjects affected / exposed	1 / 452 (0.22%)	3 / 461 (0.65%)
occurrences (all)	1	8
Hypersomnia		
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)
occurrences (all)	1	0
Hypoaesthesia		
subjects affected / exposed	9 / 452 (1.99%)	14 / 461 (3.04%)
occurrences (all)	14	23
Hypogeusia		

subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)
occurrences (all)	1	0
Hyporeflexia		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Intracranial pressure increased		
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)
occurrences (all)	1	0
Lethargy		
subjects affected / exposed	5 / 452 (1.11%)	2 / 461 (0.43%)
occurrences (all)	7	2
Loss of consciousness		
subjects affected / exposed	0 / 452 (0.00%)	3 / 461 (0.65%)
occurrences (all)	0	4
Memory impairment		
subjects affected / exposed	0 / 452 (0.00%)	4 / 461 (0.87%)
occurrences (all)	0	5
Migraine		
subjects affected / exposed	0 / 452 (0.00%)	2 / 461 (0.43%)
occurrences (all)	0	2
Migraine with aura		
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)
occurrences (all)	1	0
Myasthenia gravis		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Neuralgia		
subjects affected / exposed	2 / 452 (0.44%)	3 / 461 (0.65%)
occurrences (all)	2	4
Neurological symptom		
subjects affected / exposed	1 / 452 (0.22%)	1 / 461 (0.22%)
occurrences (all)	1	1
Neuropathy peripheral		
subjects affected / exposed	76 / 452 (16.81%)	100 / 461 (21.69%)
occurrences (all)	143	164
Neuropathy vitamin b6 deficiency		

subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)
occurrences (all)	1	0
Neurotoxicity		
subjects affected / exposed	15 / 452 (3.32%)	14 / 461 (3.04%)
occurrences (all)	27	17
Nystagmus		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	3
Olfactory nerve disorder		
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)
occurrences (all)	1	0
Paraesthesia		
subjects affected / exposed	42 / 452 (9.29%)	46 / 461 (9.98%)
occurrences (all)	57	77
Parosmia		
subjects affected / exposed	1 / 452 (0.22%)	1 / 461 (0.22%)
occurrences (all)	1	1
Peripheral motor neuropathy		
subjects affected / exposed	2 / 452 (0.44%)	5 / 461 (1.08%)
occurrences (all)	4	11
Peripheral sensory neuropathy		
subjects affected / exposed	33 / 452 (7.30%)	45 / 461 (9.76%)
occurrences (all)	49	81
Polyneuropathy		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Presyncope		
subjects affected / exposed	2 / 452 (0.44%)	4 / 461 (0.87%)
occurrences (all)	2	5
Radiculopathy		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	2
Restless legs syndrome		
subjects affected / exposed	7 / 452 (1.55%)	8 / 461 (1.74%)
occurrences (all)	9	11
Sciatica		

subjects affected / exposed	3 / 452 (0.66%)	2 / 461 (0.43%)
occurrences (all)	3	2
Seizure		
subjects affected / exposed	1 / 452 (0.22%)	1 / 461 (0.22%)
occurrences (all)	1	1
Sensorimotor disorder		
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)
occurrences (all)	1	0
Sensory disturbance		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Sensory loss		
subjects affected / exposed	1 / 452 (0.22%)	1 / 461 (0.22%)
occurrences (all)	1	1
Sinus headache		
subjects affected / exposed	2 / 452 (0.44%)	0 / 461 (0.00%)
occurrences (all)	2	0
Somnolence		
subjects affected / exposed	4 / 452 (0.88%)	7 / 461 (1.52%)
occurrences (all)	4	7
Speech disorder		
subjects affected / exposed	2 / 452 (0.44%)	0 / 461 (0.00%)
occurrences (all)	2	0
Stupor		
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)
occurrences (all)	1	0
Syncope		
subjects affected / exposed	3 / 452 (0.66%)	5 / 461 (1.08%)
occurrences (all)	4	6
Tension headache		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Tremor		
subjects affected / exposed	3 / 452 (0.66%)	6 / 461 (1.30%)
occurrences (all)	3	6
Unresponsive to stimuli		

subjects affected / exposed occurrences (all)	0 / 452 (0.00%) 0	1 / 461 (0.22%) 1	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	91 / 452 (20.13%)	50 / 461 (10.85%)	
occurrences (all)	178	94	
Anaemia folate deficiency			
subjects affected / exposed	1 / 452 (0.22%)	1 / 461 (0.22%)	
occurrences (all)	1	1	
Coagulopathy			
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)	
occurrences (all)	0	1	
Febrile neutropenia			
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)	
occurrences (all)	0	1	
Haematotoxicity			
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)	
occurrences (all)	1	0	
Iron deficiency anaemia			
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)	
occurrences (all)	2	0	
Leukocytosis			
subjects affected / exposed	1 / 452 (0.22%)	1 / 461 (0.22%)	
occurrences (all)	1	2	
Leukopenia			
subjects affected / exposed	43 / 452 (9.51%)	38 / 461 (8.24%)	
occurrences (all)	103	108	
Lymph node pain			
subjects affected / exposed	1 / 452 (0.22%)	1 / 461 (0.22%)	
occurrences (all)	1	1	
Lymphadenopathy			
subjects affected / exposed	2 / 452 (0.44%)	4 / 461 (0.87%)	
occurrences (all)	2	5	
Lymphopenia			
subjects affected / exposed	6 / 452 (1.33%)	7 / 461 (1.52%)	
occurrences (all)	8	11	

Neutropenia			
subjects affected / exposed	129 / 452 (28.54%)	102 / 461 (22.13%)	
occurrences (all)	465	310	
Sideroblastic anaemia			
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)	
occurrences (all)	1	0	
Thrombocytopenia			
subjects affected / exposed	13 / 452 (2.88%)	15 / 461 (3.25%)	
occurrences (all)	23	17	
Thrombocytosis			
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)	
occurrences (all)	0	1	
White blood cell disorder			
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)	
occurrences (all)	0	2	
Ear and labyrinth disorders			
Deafness			
subjects affected / exposed	1 / 452 (0.22%)	2 / 461 (0.43%)	
occurrences (all)	1	3	
Ear discomfort			
subjects affected / exposed	0 / 452 (0.00%)	2 / 461 (0.43%)	
occurrences (all)	0	2	
Ear pain			
subjects affected / exposed	6 / 452 (1.33%)	6 / 461 (1.30%)	
occurrences (all)	6	6	
External ear pain			
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)	
occurrences (all)	0	1	
Hypoacusis			
subjects affected / exposed	2 / 452 (0.44%)	6 / 461 (1.30%)	
occurrences (all)	2	6	
Tinnitus			
subjects affected / exposed	5 / 452 (1.11%)	9 / 461 (1.95%)	
occurrences (all)	7	12	
Vertigo			

subjects affected / exposed occurrences (all)	6 / 452 (1.33%) 7	9 / 461 (1.95%) 10	
Vertigo positional subjects affected / exposed occurrences (all)	0 / 452 (0.00%) 0	1 / 461 (0.22%) 1	
Eye disorders			
Abnormal sensation in eye subjects affected / exposed occurrences (all)	0 / 452 (0.00%) 0	1 / 461 (0.22%) 1	
Amaurosis fugax subjects affected / exposed occurrences (all)	1 / 452 (0.22%) 1	2 / 461 (0.43%) 2	
Asthenopia subjects affected / exposed occurrences (all)	2 / 452 (0.44%) 2	0 / 461 (0.00%) 0	
Blepharitis subjects affected / exposed occurrences (all)	0 / 452 (0.00%) 0	2 / 461 (0.43%) 2	
Blepharospasm subjects affected / exposed occurrences (all)	2 / 452 (0.44%) 4	0 / 461 (0.00%) 0	
Cataract subjects affected / exposed occurrences (all)	4 / 452 (0.88%) 4	4 / 461 (0.87%) 4	
Conjunctival disorder subjects affected / exposed occurrences (all)	0 / 452 (0.00%) 0	1 / 461 (0.22%) 1	
Conjunctival haemorrhage subjects affected / exposed occurrences (all)	0 / 452 (0.00%) 0	1 / 461 (0.22%) 4	
Conjunctival hyperaemia subjects affected / exposed occurrences (all)	0 / 452 (0.00%) 0	1 / 461 (0.22%) 2	
Conjunctival oedema subjects affected / exposed occurrences (all)	0 / 452 (0.00%) 0	1 / 461 (0.22%) 1	

Conjunctivitis allergic		
subjects affected / exposed	2 / 452 (0.44%)	1 / 461 (0.22%)
occurrences (all)	2	1
Diabetic retinopathy		
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)
occurrences (all)	1	0
Dry eye		
subjects affected / exposed	7 / 452 (1.55%)	8 / 461 (1.74%)
occurrences (all)	7	9
Erythema of eyelid		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Eye discharge		
subjects affected / exposed	0 / 452 (0.00%)	2 / 461 (0.43%)
occurrences (all)	0	2
Eye disorder		
subjects affected / exposed	3 / 452 (0.66%)	0 / 461 (0.00%)
occurrences (all)	3	0
Eye haemorrhage		
subjects affected / exposed	2 / 452 (0.44%)	0 / 461 (0.00%)
occurrences (all)	2	0
Eye irritation		
subjects affected / exposed	0 / 452 (0.00%)	2 / 461 (0.43%)
occurrences (all)	0	2
Eye pain		
subjects affected / exposed	5 / 452 (1.11%)	9 / 461 (1.95%)
occurrences (all)	6	9
Eye pruritus		
subjects affected / exposed	2 / 452 (0.44%)	5 / 461 (1.08%)
occurrences (all)	5	5
Glaucoma		
subjects affected / exposed	0 / 452 (0.00%)	3 / 461 (0.65%)
occurrences (all)	0	3
Growth of eyelashes		
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)
occurrences (all)	1	0

Hypermetropia		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Lacrimation disorder		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Lacrimation increased		
subjects affected / exposed	7 / 452 (1.55%)	29 / 461 (6.29%)
occurrences (all)	11	34
Meibomianitis		
subjects affected / exposed	0 / 452 (0.00%)	2 / 461 (0.43%)
occurrences (all)	0	2
Ocular hyperaemia		
subjects affected / exposed	2 / 452 (0.44%)	2 / 461 (0.43%)
occurrences (all)	2	2
Ocular hypertension		
subjects affected / exposed	1 / 452 (0.22%)	1 / 461 (0.22%)
occurrences (all)	1	1
Ocular surface disease		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Optic ischaemic neuropathy		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Photophobia		
subjects affected / exposed	1 / 452 (0.22%)	1 / 461 (0.22%)
occurrences (all)	1	1
Photopsia		
subjects affected / exposed	1 / 452 (0.22%)	1 / 461 (0.22%)
occurrences (all)	1	1
Presbyopia		
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)
occurrences (all)	1	0
Retinal detachment		
subjects affected / exposed	0 / 452 (0.00%)	2 / 461 (0.43%)
occurrences (all)	0	2

Retinopathy			
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)	
occurrences (all)	2	0	
Vision blurred			
subjects affected / exposed	20 / 452 (4.42%)	31 / 461 (6.72%)	
occurrences (all)	20	38	
Visual acuity reduced			
subjects affected / exposed	5 / 452 (1.11%)	3 / 461 (0.65%)	
occurrences (all)	5	3	
Visual impairment			
subjects affected / exposed	2 / 452 (0.44%)	7 / 461 (1.52%)	
occurrences (all)	3	8	
Xerophthalmia			
subjects affected / exposed	2 / 452 (0.44%)	1 / 461 (0.22%)	
occurrences (all)	2	1	
Gastrointestinal disorders			
Abdominal adhesions			
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)	
occurrences (all)	0	1	
Abdominal discomfort			
subjects affected / exposed	14 / 452 (3.10%)	9 / 461 (1.95%)	
occurrences (all)	15	13	
Abdominal distension			
subjects affected / exposed	36 / 452 (7.96%)	51 / 461 (11.06%)	
occurrences (all)	50	76	
Abdominal mass			
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)	
occurrences (all)	0	1	
Abdominal pain			
subjects affected / exposed	130 / 452 (28.76%)	136 / 461 (29.50%)	
occurrences (all)	238	244	
Abdominal pain lower			
subjects affected / exposed	16 / 452 (3.54%)	5 / 461 (1.08%)	
occurrences (all)	18	7	
Abdominal pain upper			

subjects affected / exposed	34 / 452 (7.52%)	56 / 461 (12.15%)
occurrences (all)	43	73
Abdominal rigidity		
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)
occurrences (all)	1	0
Abdominal wall mass		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Abnormal faeces		
subjects affected / exposed	1 / 452 (0.22%)	1 / 461 (0.22%)
occurrences (all)	1	1
Aerophagia		
subjects affected / exposed	0 / 452 (0.00%)	2 / 461 (0.43%)
occurrences (all)	0	2
Anal fissure		
subjects affected / exposed	1 / 452 (0.22%)	1 / 461 (0.22%)
occurrences (all)	1	1
Anal incontinence		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	2
Anal inflammation		
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)
occurrences (all)	1	0
Anal ulcer		
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)
occurrences (all)	1	0
Anorectal discomfort		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	2
Anorectal disorder		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Aphthous ulcer		
subjects affected / exposed	1 / 452 (0.22%)	3 / 461 (0.65%)
occurrences (all)	1	6
Aptyalism		

subjects affected / exposed	0 / 452 (0.00%)	2 / 461 (0.43%)
occurrences (all)	0	4
Ascites		
subjects affected / exposed	55 / 452 (12.17%)	96 / 461 (20.82%)
occurrences (all)	94	222
Bowel movement irregularity		
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)
occurrences (all)	1	0
Breath odour		
subjects affected / exposed	0 / 452 (0.00%)	3 / 461 (0.65%)
occurrences (all)	0	4
Change of bowel habit		
subjects affected / exposed	1 / 452 (0.22%)	1 / 461 (0.22%)
occurrences (all)	1	1
Cheilitis		
subjects affected / exposed	2 / 452 (0.44%)	0 / 461 (0.00%)
occurrences (all)	2	0
Coeliac disease		
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)
occurrences (all)	1	0
Colitis		
subjects affected / exposed	1 / 452 (0.22%)	1 / 461 (0.22%)
occurrences (all)	1	1
Colonic fistula		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Constipation		
subjects affected / exposed	134 / 452 (29.65%)	110 / 461 (23.86%)
occurrences (all)	187	174
Defaecation urgency		
subjects affected / exposed	3 / 452 (0.66%)	3 / 461 (0.65%)
occurrences (all)	3	3
Dental caries		
subjects affected / exposed	4 / 452 (0.88%)	3 / 461 (0.65%)
occurrences (all)	4	3
Diaphragmatic hernia		

subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Diarrhoea		
subjects affected / exposed	123 / 452 (27.21%)	140 / 461 (30.37%)
occurrences (all)	214	297
Diarrhoea haemorrhagic		
subjects affected / exposed	1 / 452 (0.22%)	1 / 461 (0.22%)
occurrences (all)	1	2
Diverticulum intestinal		
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)
occurrences (all)	1	0
Dry mouth		
subjects affected / exposed	18 / 452 (3.98%)	10 / 461 (2.17%)
occurrences (all)	21	14
Duodenitis		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Dyspepsia		
subjects affected / exposed	39 / 452 (8.63%)	47 / 461 (10.20%)
occurrences (all)	48	80
Dysphagia		
subjects affected / exposed	4 / 452 (0.88%)	7 / 461 (1.52%)
occurrences (all)	4	8
Enterovesical fistula		
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)
occurrences (all)	1	0
Epigastric discomfort		
subjects affected / exposed	0 / 452 (0.00%)	2 / 461 (0.43%)
occurrences (all)	0	2
Eructation		
subjects affected / exposed	1 / 452 (0.22%)	3 / 461 (0.65%)
occurrences (all)	1	3
Faecal vomiting		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Faecaloma		

subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)
occurrences (all)	1	0
Faeces discoloured		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Faeces soft		
subjects affected / exposed	1 / 452 (0.22%)	2 / 461 (0.43%)
occurrences (all)	1	3
Flatulence		
subjects affected / exposed	19 / 452 (4.20%)	20 / 461 (4.34%)
occurrences (all)	23	28
Frequent bowel movements		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Gastritis		
subjects affected / exposed	5 / 452 (1.11%)	4 / 461 (0.87%)
occurrences (all)	6	5
Gastrointestinal disorder		
subjects affected / exposed	1 / 452 (0.22%)	3 / 461 (0.65%)
occurrences (all)	1	3
Gastrointestinal haemorrhage		
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)
occurrences (all)	1	0
Gastrointestinal motility disorder		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Gastrointestinal obstruction		
subjects affected / exposed	0 / 452 (0.00%)	2 / 461 (0.43%)
occurrences (all)	0	2
Gastrointestinal pain		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Gastrointestinal sounds abnormal		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Gastrooesophageal reflux disease		

subjects affected / exposed	20 / 452 (4.42%)	23 / 461 (4.99%)
occurrences (all)	30	38
Gingival bleeding		
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)
occurrences (all)	1	0
Gingival discomfort		
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)
occurrences (all)	1	0
Gingival pain		
subjects affected / exposed	6 / 452 (1.33%)	1 / 461 (0.22%)
occurrences (all)	10	1
Gingival ulceration		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Glossitis		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Haematemesis		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Haemorrhoidal haemorrhage		
subjects affected / exposed	2 / 452 (0.44%)	0 / 461 (0.00%)
occurrences (all)	3	0
Haemorrhoids		
subjects affected / exposed	9 / 452 (1.99%)	15 / 461 (3.25%)
occurrences (all)	11	18
Hernial eventration		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Hiatus hernia		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Hyperchlorhydria		
subjects affected / exposed	1 / 452 (0.22%)	2 / 461 (0.43%)
occurrences (all)	2	2
Hypoaesthesia oral		

subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)
occurrences (all)	1	0
Hypoaesthesia teeth		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Ileus		
subjects affected / exposed	2 / 452 (0.44%)	6 / 461 (1.30%)
occurrences (all)	2	6
Impaired gastric emptying		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Intestinal obstruction		
subjects affected / exposed	3 / 452 (0.66%)	7 / 461 (1.52%)
occurrences (all)	3	8
Intra-abdominal fluid collection		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Large intestinal haemorrhage		
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)
occurrences (all)	1	0
Large intestinal stenosis		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Lip blister		
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)
occurrences (all)	1	0
Lip dry		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Loose tooth		
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)
occurrences (all)	1	0
Mouth ulceration		
subjects affected / exposed	6 / 452 (1.33%)	6 / 461 (1.30%)
occurrences (all)	7	8
Nausea		

subjects affected / exposed	176 / 452 (38.94%)	190 / 461 (41.21%)
occurrences (all)	301	337
Odynophagia		
subjects affected / exposed	4 / 452 (0.88%)	1 / 461 (0.22%)
occurrences (all)	5	1
Oesophageal pain		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Oesophageal spasm		
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)
occurrences (all)	1	0
Oesophagitis		
subjects affected / exposed	3 / 452 (0.66%)	2 / 461 (0.43%)
occurrences (all)	3	2
Oral discomfort		
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)
occurrences (all)	1	0
Oral pain		
subjects affected / exposed	3 / 452 (0.66%)	3 / 461 (0.65%)
occurrences (all)	3	3
Paraesthesia oral		
subjects affected / exposed	0 / 452 (0.00%)	4 / 461 (0.87%)
occurrences (all)	0	4
Perianal erythema		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Periodontal disease		
subjects affected / exposed	2 / 452 (0.44%)	1 / 461 (0.22%)
occurrences (all)	2	2
Proctalgia		
subjects affected / exposed	1 / 452 (0.22%)	1 / 461 (0.22%)
occurrences (all)	1	1
Proctitis		
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)
occurrences (all)	1	0
Rectal haemorrhage		

subjects affected / exposed	11 / 452 (2.43%)	3 / 461 (0.65%)
occurrences (all)	13	3
Rectal obstruction		
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)
occurrences (all)	1	0
Rectal tenesmus		
subjects affected / exposed	3 / 452 (0.66%)	1 / 461 (0.22%)
occurrences (all)	4	2
Regurgitation		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	2
Retching		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Salivary gland disorder		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Salivary hypersecretion		
subjects affected / exposed	2 / 452 (0.44%)	0 / 461 (0.00%)
occurrences (all)	3	0
Sensitivity of teeth		
subjects affected / exposed	0 / 452 (0.00%)	3 / 461 (0.65%)
occurrences (all)	0	6
Small intestinal obstruction		
subjects affected / exposed	1 / 452 (0.22%)	2 / 461 (0.43%)
occurrences (all)	1	2
Stomatitis		
subjects affected / exposed	26 / 452 (5.75%)	20 / 461 (4.34%)
occurrences (all)	39	30
Subileus		
subjects affected / exposed	3 / 452 (0.66%)	6 / 461 (1.30%)
occurrences (all)	3	8
Tongue coated		
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)
occurrences (all)	1	0
Tongue discolouration		

subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)	
occurrences (all)	0	1	
Tongue discomfort			
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)	
occurrences (all)	0	1	
Tongue disorder			
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)	
occurrences (all)	0	1	
Tongue ulceration			
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)	
occurrences (all)	0	1	
Tooth demineralisation			
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)	
occurrences (all)	1	0	
Tooth disorder			
subjects affected / exposed	0 / 452 (0.00%)	2 / 461 (0.43%)	
occurrences (all)	0	3	
Toothache			
subjects affected / exposed	10 / 452 (2.21%)	12 / 461 (2.60%)	
occurrences (all)	10	12	
Ulcerative gastritis			
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)	
occurrences (all)	0	1	
Umbilical hernia			
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)	
occurrences (all)	0	1	
Vomiting			
subjects affected / exposed	102 / 452 (22.57%)	122 / 461 (26.46%)	
occurrences (all)	190	199	
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	0 / 452 (0.00%)	6 / 461 (1.30%)	
occurrences (all)	0	11	
Alopecia			
subjects affected / exposed	166 / 452 (36.73%)	155 / 461 (33.62%)	
occurrences (all)	199	186	

Alopecia areata		
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)
occurrences (all)	1	0
Alopecia totalis		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Blister		
subjects affected / exposed	2 / 452 (0.44%)	9 / 461 (1.95%)
occurrences (all)	2	10
Chloasma		
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)
occurrences (all)	1	0
Cold sweat		
subjects affected / exposed	0 / 452 (0.00%)	2 / 461 (0.43%)
occurrences (all)	0	3
Dermatitis		
subjects affected / exposed	3 / 452 (0.66%)	3 / 461 (0.65%)
occurrences (all)	4	5
Dermatitis acneiform		
subjects affected / exposed	1 / 452 (0.22%)	2 / 461 (0.43%)
occurrences (all)	1	2
Dermatitis allergic		
subjects affected / exposed	0 / 452 (0.00%)	2 / 461 (0.43%)
occurrences (all)	0	3
Dermatitis contact		
subjects affected / exposed	3 / 452 (0.66%)	1 / 461 (0.22%)
occurrences (all)	4	1
Dry skin		
subjects affected / exposed	11 / 452 (2.43%)	25 / 461 (5.42%)
occurrences (all)	13	33
Ecchymosis		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Eczema		
subjects affected / exposed	2 / 452 (0.44%)	5 / 461 (1.08%)
occurrences (all)	2	5

Eczema asteatotic		
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)
occurrences (all)	1	0
Erythema		
subjects affected / exposed	29 / 452 (6.42%)	27 / 461 (5.86%)
occurrences (all)	56	49
Erythema nodosum		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Exfoliative rash		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Haemorrhage subcutaneous		
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)
occurrences (all)	1	0
Hair disorder		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Hand dermatitis		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Hyperhidrosis		
subjects affected / exposed	3 / 452 (0.66%)	6 / 461 (1.30%)
occurrences (all)	6	6
Hyperkeratosis		
subjects affected / exposed	2 / 452 (0.44%)	5 / 461 (1.08%)
occurrences (all)	2	7
Ingrowing nail		
subjects affected / exposed	1 / 452 (0.22%)	2 / 461 (0.43%)
occurrences (all)	1	2
Intertrigo		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Livedo reticularis		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1

Miliaria		
subjects affected / exposed	1 / 452 (0.22%)	2 / 461 (0.43%)
occurrences (all)	1	2
Nail bed disorder		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Nail bed inflammation		
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)
occurrences (all)	3	0
Nail discolouration		
subjects affected / exposed	8 / 452 (1.77%)	7 / 461 (1.52%)
occurrences (all)	9	9
Nail discomfort		
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)
occurrences (all)	1	0
Nail disorder		
subjects affected / exposed	33 / 452 (7.30%)	34 / 461 (7.38%)
occurrences (all)	39	57
Nail dystrophy		
subjects affected / exposed	3 / 452 (0.66%)	5 / 461 (1.08%)
occurrences (all)	4	9
Nail pigmentation		
subjects affected / exposed	0 / 452 (0.00%)	2 / 461 (0.43%)
occurrences (all)	0	2
Nail ridging		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Nail toxicity		
subjects affected / exposed	1 / 452 (0.22%)	6 / 461 (1.30%)
occurrences (all)	1	10
Night sweats		
subjects affected / exposed	2 / 452 (0.44%)	2 / 461 (0.43%)
occurrences (all)	2	3
Onychalgia		
subjects affected / exposed	3 / 452 (0.66%)	5 / 461 (1.08%)
occurrences (all)	3	7

Onychoclasia		
subjects affected / exposed	1 / 452 (0.22%)	3 / 461 (0.65%)
occurrences (all)	2	4
Onycholysis		
subjects affected / exposed	8 / 452 (1.77%)	15 / 461 (3.25%)
occurrences (all)	18	30
Onychomadesis		
subjects affected / exposed	2 / 452 (0.44%)	2 / 461 (0.43%)
occurrences (all)	2	2
Pain of skin		
subjects affected / exposed	4 / 452 (0.88%)	2 / 461 (0.43%)
occurrences (all)	4	2
Palmar erythema		
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)
occurrences (all)	1	0
Palmar-plantar erythrodysesthesia syndrome		
subjects affected / exposed	3 / 452 (0.66%)	6 / 461 (1.30%)
occurrences (all)	3	7
Perivascular dermatitis		
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)
occurrences (all)	1	0
Peau d'orange		
subjects affected / exposed	0 / 452 (0.00%)	2 / 461 (0.43%)
occurrences (all)	0	2
Petechiae		
subjects affected / exposed	1 / 452 (0.22%)	1 / 461 (0.22%)
occurrences (all)	1	1
Photosensitivity reaction		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	2
Pigmentation disorder		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Pruritus		

subjects affected / exposed	35 / 452 (7.74%)	29 / 461 (6.29%)
occurrences (all)	48	38
Pruritus generalised		
subjects affected / exposed	5 / 452 (1.11%)	3 / 461 (0.65%)
occurrences (all)	5	3
Purpura		
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)
occurrences (all)	2	0
Rash erythematous		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Rash		
subjects affected / exposed	50 / 452 (11.06%)	31 / 461 (6.72%)
occurrences (all)	82	41
Rash generalised		
subjects affected / exposed	2 / 452 (0.44%)	1 / 461 (0.22%)
occurrences (all)	3	1
Rash macular		
subjects affected / exposed	2 / 452 (0.44%)	0 / 461 (0.00%)
occurrences (all)	2	0
Rash maculo-papular		
subjects affected / exposed	4 / 452 (0.88%)	3 / 461 (0.65%)
occurrences (all)	6	3
Rash papular		
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)
occurrences (all)	2	0
Rash pruritic		
subjects affected / exposed	2 / 452 (0.44%)	1 / 461 (0.22%)
occurrences (all)	2	1
Rash vesicular		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Skin atrophy		
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)
occurrences (all)	1	0
Skin burning sensation		

subjects affected / exposed	0 / 452 (0.00%)	2 / 461 (0.43%)
occurrences (all)	0	2
Skin depigmentation		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Skin discolouration		
subjects affected / exposed	4 / 452 (0.88%)	4 / 461 (0.87%)
occurrences (all)	4	4
Skin disorder		
subjects affected / exposed	2 / 452 (0.44%)	3 / 461 (0.65%)
occurrences (all)	2	5
Skin exfoliation		
subjects affected / exposed	1 / 452 (0.22%)	1 / 461 (0.22%)
occurrences (all)	1	2
Skin fissures		
subjects affected / exposed	0 / 452 (0.00%)	7 / 461 (1.52%)
occurrences (all)	0	14
Skin hyperpigmentation		
subjects affected / exposed	1 / 452 (0.22%)	4 / 461 (0.87%)
occurrences (all)	1	4
Skin hypertrophy		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Skin induration		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Skin irritation		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Skin lesion		
subjects affected / exposed	5 / 452 (1.11%)	11 / 461 (2.39%)
occurrences (all)	6	11
Skin maceration		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Skin mass		

subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)	
occurrences (all)	0	1	
Skin reaction			
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)	
occurrences (all)	1	0	
Skin ulcer			
subjects affected / exposed	0 / 452 (0.00%)	2 / 461 (0.43%)	
occurrences (all)	0	3	
Swelling face			
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)	
occurrences (all)	0	1	
Telangiectasia			
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)	
occurrences (all)	1	0	
Toxic skin eruption			
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)	
occurrences (all)	5	0	
Umbilical haemorrhage			
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)	
occurrences (all)	0	2	
Urticaria			
subjects affected / exposed	5 / 452 (1.11%)	1 / 461 (0.22%)	
occurrences (all)	6	1	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	2 / 452 (0.44%)	1 / 461 (0.22%)	
occurrences (all)	2	1	
Anuria			
subjects affected / exposed	1 / 452 (0.22%)	1 / 461 (0.22%)	
occurrences (all)	1	1	
Azotaemia			
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)	
occurrences (all)	1	0	
Bladder spasm			
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)	
occurrences (all)	0	1	

Dysuria		
subjects affected / exposed	16 / 452 (3.54%)	22 / 461 (4.77%)
occurrences (all)	21	27
Haematuria		
subjects affected / exposed	6 / 452 (1.33%)	3 / 461 (0.65%)
occurrences (all)	8	3
Haemorrhage urinary tract		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Hydronephrosis		
subjects affected / exposed	3 / 452 (0.66%)	6 / 461 (1.30%)
occurrences (all)	3	6
Hydroureter		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Incontinence		
subjects affected / exposed	1 / 452 (0.22%)	2 / 461 (0.43%)
occurrences (all)	1	2
Leukocyturia		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Lower urinary tract symptoms		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Micturition urgency		
subjects affected / exposed	1 / 452 (0.22%)	3 / 461 (0.65%)
occurrences (all)	1	3
Nephropathy toxic		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Nocturia		
subjects affected / exposed	3 / 452 (0.66%)	1 / 461 (0.22%)
occurrences (all)	3	1
Obstructive uropathy		
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)
occurrences (all)	1	0

Oliguria		
subjects affected / exposed	1 / 452 (0.22%)	2 / 461 (0.43%)
occurrences (all)	1	2
Pollakiuria		
subjects affected / exposed	12 / 452 (2.65%)	9 / 461 (1.95%)
occurrences (all)	15	10
Polyuria		
subjects affected / exposed	1 / 452 (0.22%)	1 / 461 (0.22%)
occurrences (all)	1	2
Proteinuria		
subjects affected / exposed	12 / 452 (2.65%)	18 / 461 (3.90%)
occurrences (all)	18	29
Pyelocaliectasis		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Renal colic		
subjects affected / exposed	0 / 452 (0.00%)	3 / 461 (0.65%)
occurrences (all)	0	3
Renal failure		
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)
occurrences (all)	1	0
Renal pain		
subjects affected / exposed	0 / 452 (0.00%)	3 / 461 (0.65%)
occurrences (all)	0	3
Stress urinary incontinence		
subjects affected / exposed	1 / 452 (0.22%)	2 / 461 (0.43%)
occurrences (all)	1	2
Ureteric obstruction		
subjects affected / exposed	2 / 452 (0.44%)	0 / 461 (0.00%)
occurrences (all)	2	0
Urethral pain		
subjects affected / exposed	1 / 452 (0.22%)	1 / 461 (0.22%)
occurrences (all)	1	1
Urinary hesitation		
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)
occurrences (all)	1	0

Urinary incontinence subjects affected / exposed occurrences (all)	7 / 452 (1.55%) 7	4 / 461 (0.87%) 27	
Urinary retention subjects affected / exposed occurrences (all)	0 / 452 (0.00%) 0	2 / 461 (0.43%) 2	
Urinary tract disorder subjects affected / exposed occurrences (all)	1 / 452 (0.22%) 1	0 / 461 (0.00%) 0	
Urinary tract obstruction subjects affected / exposed occurrences (all)	1 / 452 (0.22%) 1	0 / 461 (0.00%) 0	
Urinary tract pain subjects affected / exposed occurrences (all)	1 / 452 (0.22%) 1	0 / 461 (0.00%) 0	
Urine abnormality subjects affected / exposed occurrences (all)	0 / 452 (0.00%) 0	2 / 461 (0.43%) 5	
Vesical fistula subjects affected / exposed occurrences (all)	0 / 452 (0.00%) 0	1 / 461 (0.22%) 1	
Endocrine disorders			
Cushing's syndrome subjects affected / exposed occurrences (all)	0 / 452 (0.00%) 0	1 / 461 (0.22%) 2	
Cushingoid subjects affected / exposed occurrences (all)	0 / 452 (0.00%) 0	1 / 461 (0.22%) 1	
Goitre subjects affected / exposed occurrences (all)	0 / 452 (0.00%) 0	1 / 461 (0.22%) 1	
Hypothyroidism subjects affected / exposed occurrences (all)	0 / 452 (0.00%) 0	3 / 461 (0.65%) 3	
Musculoskeletal and connective tissue disorders			

Amyotrophy		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Arthralgia		
subjects affected / exposed	50 / 452 (11.06%)	50 / 461 (10.85%)
occurrences (all)	69	72
Arthritis		
subjects affected / exposed	1 / 452 (0.22%)	1 / 461 (0.22%)
occurrences (all)	1	1
Back pain		
subjects affected / exposed	65 / 452 (14.38%)	56 / 461 (12.15%)
occurrences (all)	76	79
Bone pain		
subjects affected / exposed	13 / 452 (2.88%)	14 / 461 (3.04%)
occurrences (all)	22	21
Chondromalacia		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Exostosis		
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)
occurrences (all)	1	0
Fistula		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Flank pain		
subjects affected / exposed	6 / 452 (1.33%)	7 / 461 (1.52%)
occurrences (all)	6	11
Groin pain		
subjects affected / exposed	10 / 452 (2.21%)	12 / 461 (2.60%)
occurrences (all)	11	15
Hypercreatinaemia		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	2
Inguinal mass		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1

Intervertebral disc protrusion subjects affected / exposed occurrences (all)	0 / 452 (0.00%) 0	1 / 461 (0.22%) 1
Joint effusion subjects affected / exposed occurrences (all)	0 / 452 (0.00%) 0	1 / 461 (0.22%) 1
Joint stiffness subjects affected / exposed occurrences (all)	1 / 452 (0.22%) 1	2 / 461 (0.43%) 3
Limb discomfort subjects affected / exposed occurrences (all)	0 / 452 (0.00%) 0	5 / 461 (1.08%) 5
Muscle atrophy subjects affected / exposed occurrences (all)	1 / 452 (0.22%) 1	0 / 461 (0.00%) 0
Muscle contracture subjects affected / exposed occurrences (all)	2 / 452 (0.44%) 2	1 / 461 (0.22%) 1
Muscle hypertrophy subjects affected / exposed occurrences (all)	1 / 452 (0.22%) 1	0 / 461 (0.00%) 0
Muscle spasms subjects affected / exposed occurrences (all)	30 / 452 (6.64%) 40	18 / 461 (3.90%) 22
Muscle tightness subjects affected / exposed occurrences (all)	1 / 452 (0.22%) 1	0 / 461 (0.00%) 0
Muscle twitching subjects affected / exposed occurrences (all)	1 / 452 (0.22%) 1	1 / 461 (0.22%) 1
Muscular weakness subjects affected / exposed occurrences (all)	12 / 452 (2.65%) 13	15 / 461 (3.25%) 17
Musculoskeletal chest pain subjects affected / exposed occurrences (all)	7 / 452 (1.55%) 8	12 / 461 (2.60%) 14

Musculoskeletal discomfort		
subjects affected / exposed	1 / 452 (0.22%)	3 / 461 (0.65%)
occurrences (all)	1	4
Musculoskeletal pain		
subjects affected / exposed	18 / 452 (3.98%)	25 / 461 (5.42%)
occurrences (all)	25	34
Musculoskeletal stiffness		
subjects affected / exposed	1 / 452 (0.22%)	3 / 461 (0.65%)
occurrences (all)	1	3
Myalgia		
subjects affected / exposed	48 / 452 (10.62%)	49 / 461 (10.63%)
occurrences (all)	71	64
Neck mass		
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)
occurrences (all)	1	0
Neck pain		
subjects affected / exposed	5 / 452 (1.11%)	10 / 461 (2.17%)
occurrences (all)	6	16
Osteoarthritis		
subjects affected / exposed	3 / 452 (0.66%)	4 / 461 (0.87%)
occurrences (all)	5	5
Osteonecrosis		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Osteopenia		
subjects affected / exposed	0 / 452 (0.00%)	2 / 461 (0.43%)
occurrences (all)	0	2
Osteoporotic fracture		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Pain in extremity		
subjects affected / exposed	44 / 452 (9.73%)	53 / 461 (11.50%)
occurrences (all)	69	82
Pain in jaw		
subjects affected / exposed	1 / 452 (0.22%)	5 / 461 (1.08%)
occurrences (all)	2	6

Pathological fracture		
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)
occurrences (all)	1	0
Plantar fasciitis		
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)
occurrences (all)	1	0
Posture abnormal		
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)
occurrences (all)	2	0
Pubic pain		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Rotator cuff syndrome		
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)
occurrences (all)	1	0
Scleroderma		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	2
Scoliosis		
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)
occurrences (all)	1	0
Spinal osteoarthritis		
subjects affected / exposed	2 / 452 (0.44%)	1 / 461 (0.22%)
occurrences (all)	2	1
Spinal pain		
subjects affected / exposed	3 / 452 (0.66%)	2 / 461 (0.43%)
occurrences (all)	4	3
Spondylolisthesis		
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)
occurrences (all)	1	0
Temporomandibular joint syndrome		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Tendon disorder		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1

Tendonitis			
subjects affected / exposed	1 / 452 (0.22%)	1 / 461 (0.22%)	
occurrences (all)	1	1	
Trigger finger			
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)	
occurrences (all)	1	0	
Trismus			
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)	
occurrences (all)	3	0	
Infections and infestations			
Abdominal infection			
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)	
occurrences (all)	0	1	
Abdominal sepsis			
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)	
occurrences (all)	1	0	
Anal abscess			
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)	
occurrences (all)	0	1	
Angular cheilitis			
subjects affected / exposed	0 / 452 (0.00%)	4 / 461 (0.87%)	
occurrences (all)	0	6	
Aspergillus infection			
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)	
occurrences (all)	0	2	
Bacterial infection			
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)	
occurrences (all)	1	0	
Breast abscess			
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)	
occurrences (all)	1	0	
Bronchitis			
subjects affected / exposed	9 / 452 (1.99%)	14 / 461 (3.04%)	
occurrences (all)	11	15	
Candida infection			

subjects affected / exposed	1 / 452 (0.22%)	1 / 461 (0.22%)
occurrences (all)	1	1
Catheter site cellulitis		
subjects affected / exposed	2 / 452 (0.44%)	0 / 461 (0.00%)
occurrences (all)	2	0
Catheter site infection		
subjects affected / exposed	1 / 452 (0.22%)	4 / 461 (0.87%)
occurrences (all)	1	4
Cellulitis		
subjects affected / exposed	4 / 452 (0.88%)	4 / 461 (0.87%)
occurrences (all)	5	6
Chronic sinusitis		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Conjunctivitis		
subjects affected / exposed	9 / 452 (1.99%)	6 / 461 (1.30%)
occurrences (all)	9	6
Conjunctivitis bacterial		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Conjunctivitis viral		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Cystitis		
subjects affected / exposed	13 / 452 (2.88%)	17 / 461 (3.69%)
occurrences (all)	16	21
Cystitis klebsiella		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Device related infection		
subjects affected / exposed	1 / 452 (0.22%)	4 / 461 (0.87%)
occurrences (all)	1	6
Diarrhoea infectious		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Disseminated bacillus calmette-		

guerin infection		
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)
occurrences (all)	1	0
Ear infection		
subjects affected / exposed	1 / 452 (0.22%)	2 / 461 (0.43%)
occurrences (all)	1	2
Echinococciasis		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Empyema		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Enterocolitis infectious		
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)
occurrences (all)	1	0
Erysipelas		
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)
occurrences (all)	1	0
Escherichia urinary tract infection		
subjects affected / exposed	2 / 452 (0.44%)	0 / 461 (0.00%)
occurrences (all)	2	0
Eye infection		
subjects affected / exposed	1 / 452 (0.22%)	3 / 461 (0.65%)
occurrences (all)	1	4
Folliculitis		
subjects affected / exposed	2 / 452 (0.44%)	3 / 461 (0.65%)
occurrences (all)	2	3
Fungal infection		
subjects affected / exposed	4 / 452 (0.88%)	3 / 461 (0.65%)
occurrences (all)	4	3
Fungal skin infection		
subjects affected / exposed	0 / 452 (0.00%)	6 / 461 (1.30%)
occurrences (all)	0	6
Furuncle		
subjects affected / exposed	2 / 452 (0.44%)	0 / 461 (0.00%)
occurrences (all)	2	0

Gastroenteritis		
subjects affected / exposed	6 / 452 (1.33%)	7 / 461 (1.52%)
occurrences (all)	6	7
Gastroenteritis viral		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Gastrointestinal infection		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Genital herpes		
subjects affected / exposed	2 / 452 (0.44%)	0 / 461 (0.00%)
occurrences (all)	4	0
Gingival abscess		
subjects affected / exposed	1 / 452 (0.22%)	1 / 461 (0.22%)
occurrences (all)	1	1
Gingivitis		
subjects affected / exposed	3 / 452 (0.66%)	2 / 461 (0.43%)
occurrences (all)	3	2
Helicobacter infection		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Herpes dermatitis		
subjects affected / exposed	2 / 452 (0.44%)	0 / 461 (0.00%)
occurrences (all)	2	0
Herpes simplex		
subjects affected / exposed	1 / 452 (0.22%)	2 / 461 (0.43%)
occurrences (all)	1	2
Herpes virus infection		
subjects affected / exposed	2 / 452 (0.44%)	7 / 461 (1.52%)
occurrences (all)	3	7
Herpes zoster		
subjects affected / exposed	4 / 452 (0.88%)	3 / 461 (0.65%)
occurrences (all)	4	4
Hordeolum		
subjects affected / exposed	2 / 452 (0.44%)	2 / 461 (0.43%)
occurrences (all)	2	2

Infection		
subjects affected / exposed	3 / 452 (0.66%)	7 / 461 (1.52%)
occurrences (all)	3	8
Influenza		
subjects affected / exposed	10 / 452 (2.21%)	8 / 461 (1.74%)
occurrences (all)	10	11
Injection site infection		
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)
occurrences (all)	1	0
Klebsiella infection		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Laryngitis		
subjects affected / exposed	3 / 452 (0.66%)	2 / 461 (0.43%)
occurrences (all)	3	2
Localised infection		
subjects affected / exposed	3 / 452 (0.66%)	3 / 461 (0.65%)
occurrences (all)	5	4
Lower respiratory tract infection		
subjects affected / exposed	4 / 452 (0.88%)	3 / 461 (0.65%)
occurrences (all)	4	4
Lung infection		
subjects affected / exposed	2 / 452 (0.44%)	1 / 461 (0.22%)
occurrences (all)	2	1
Nail bed infection		
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)
occurrences (all)	1	0
Nail infection		
subjects affected / exposed	2 / 452 (0.44%)	2 / 461 (0.43%)
occurrences (all)	2	9
Nasopharyngitis		
subjects affected / exposed	29 / 452 (6.42%)	57 / 461 (12.36%)
occurrences (all)	54	71
Onychomycosis		
subjects affected / exposed	2 / 452 (0.44%)	2 / 461 (0.43%)
occurrences (all)	2	2

Oral candidiasis		
subjects affected / exposed	2 / 452 (0.44%)	6 / 461 (1.30%)
occurrences (all)	2	6
Oral fungal infection		
subjects affected / exposed	1 / 452 (0.22%)	2 / 461 (0.43%)
occurrences (all)	2	2
Oral herpes		
subjects affected / exposed	8 / 452 (1.77%)	13 / 461 (2.82%)
occurrences (all)	10	17
Oral infection		
subjects affected / exposed	1 / 452 (0.22%)	2 / 461 (0.43%)
occurrences (all)	1	2
Otitis media		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	2
Paronychia		
subjects affected / exposed	1 / 452 (0.22%)	9 / 461 (1.95%)
occurrences (all)	1	11
Periodontitis		
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)
occurrences (all)	1	0
Periumbilical abscess		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Pharyngitis		
subjects affected / exposed	3 / 452 (0.66%)	5 / 461 (1.08%)
occurrences (all)	3	5
Pneumonia		
subjects affected / exposed	6 / 452 (1.33%)	7 / 461 (1.52%)
occurrences (all)	6	7
Pneumonia bacterial		
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)
occurrences (all)	1	0
Pulpitis dental		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1

Pyelonephritis		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Pyuria		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	2
Rash pustular		
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)
occurrences (all)	1	0
Respiratory syncytial virus infection		
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)
occurrences (all)	1	0
Respiratory tract infection		
subjects affected / exposed	1 / 452 (0.22%)	8 / 461 (1.74%)
occurrences (all)	1	10
Rhinitis		
subjects affected / exposed	12 / 452 (2.65%)	19 / 461 (4.12%)
occurrences (all)	16	25
Sinusitis		
subjects affected / exposed	6 / 452 (1.33%)	4 / 461 (0.87%)
occurrences (all)	8	5
Skin bacterial infection		
subjects affected / exposed	1 / 452 (0.22%)	1 / 461 (0.22%)
occurrences (all)	1	1
Skin infection		
subjects affected / exposed	0 / 452 (0.00%)	5 / 461 (1.08%)
occurrences (all)	0	8
Soft tissue infection		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Staphylococcal sepsis		
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)
occurrences (all)	1	0
Superinfection		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1

Tinea pedis		
subjects affected / exposed	0 / 452 (0.00%)	2 / 461 (0.43%)
occurrences (all)	0	3
Tonsillitis		
subjects affected / exposed	4 / 452 (0.88%)	1 / 461 (0.22%)
occurrences (all)	4	1
Tooth abscess		
subjects affected / exposed	0 / 452 (0.00%)	2 / 461 (0.43%)
occurrences (all)	0	2
Tooth infection		
subjects affected / exposed	2 / 452 (0.44%)	3 / 461 (0.65%)
occurrences (all)	3	3
Tracheitis		
subjects affected / exposed	1 / 452 (0.22%)	3 / 461 (0.65%)
occurrences (all)	1	3
Tracheobronchitis		
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)
occurrences (all)	1	0
Upper respiratory tract infection		
subjects affected / exposed	17 / 452 (3.76%)	24 / 461 (5.21%)
occurrences (all)	19	36
Urinary tract infection		
subjects affected / exposed	38 / 452 (8.41%)	41 / 461 (8.89%)
occurrences (all)	48	54
Urinary tract infection bacterial		
subjects affected / exposed	4 / 452 (0.88%)	3 / 461 (0.65%)
occurrences (all)	4	3
Urinary tract infection fungal		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	2
Urosepsis		
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)
occurrences (all)	1	0
Vaginal infection		
subjects affected / exposed	2 / 452 (0.44%)	1 / 461 (0.22%)
occurrences (all)	2	1

Viral diarrhoea			
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)	
occurrences (all)	1	0	
Viral infection			
subjects affected / exposed	2 / 452 (0.44%)	2 / 461 (0.43%)	
occurrences (all)	2	3	
Vulvitis			
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)	
occurrences (all)	1	0	
Vulvovaginal candidiasis			
subjects affected / exposed	2 / 452 (0.44%)	1 / 461 (0.22%)	
occurrences (all)	2	1	
Vulvovaginal mycotic infection			
subjects affected / exposed	1 / 452 (0.22%)	3 / 461 (0.65%)	
occurrences (all)	1	3	
Wound infection			
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)	
occurrences (all)	0	1	
Metabolism and nutrition disorders			
Abnormal weight gain			
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)	
occurrences (all)	1	0	
Calcium deficiency			
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)	
occurrences (all)	0	1	
Decreased appetite			
subjects affected / exposed	81 / 452 (17.92%)	85 / 461 (18.44%)	
occurrences (all)	126	132	
Dehydration			
subjects affected / exposed	11 / 452 (2.43%)	18 / 461 (3.90%)	
occurrences (all)	15	20	
Diabetes mellitus			
subjects affected / exposed	2 / 452 (0.44%)	2 / 461 (0.43%)	
occurrences (all)	2	2	
Diabetes mellitus inadequate control			

subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)
occurrences (all)	1	0
Diabetic ketoacidosis		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Dyslipidaemia		
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)
occurrences (all)	1	0
Feeding disorder		
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)
occurrences (all)	1	0
Fluid retention		
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)
occurrences (all)	1	0
Food craving		
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)
occurrences (all)	1	0
Hypercalcaemia		
subjects affected / exposed	2 / 452 (0.44%)	2 / 461 (0.43%)
occurrences (all)	2	2
Hypercholesterolaemia		
subjects affected / exposed	3 / 452 (0.66%)	0 / 461 (0.00%)
occurrences (all)	4	0
Hyperglycaemia		
subjects affected / exposed	13 / 452 (2.88%)	9 / 461 (1.95%)
occurrences (all)	37	18
Hyperkalaemia		
subjects affected / exposed	9 / 452 (1.99%)	11 / 461 (2.39%)
occurrences (all)	19	14
Hypermagnesaemia		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Hypernatraemia		
subjects affected / exposed	1 / 452 (0.22%)	3 / 461 (0.65%)
occurrences (all)	1	3
Hypertriglyceridaemia		

subjects affected / exposed	0 / 452 (0.00%)	2 / 461 (0.43%)
occurrences (all)	0	2
Hyperuricaemia		
subjects affected / exposed	2 / 452 (0.44%)	3 / 461 (0.65%)
occurrences (all)	2	4
Hypoalbuminaemia		
subjects affected / exposed	10 / 452 (2.21%)	16 / 461 (3.47%)
occurrences (all)	12	27
Hypocalcaemia		
subjects affected / exposed	5 / 452 (1.11%)	5 / 461 (1.08%)
occurrences (all)	6	8
Hypochloraemia		
subjects affected / exposed	2 / 452 (0.44%)	2 / 461 (0.43%)
occurrences (all)	2	2
Hypoglycaemia		
subjects affected / exposed	1 / 452 (0.22%)	2 / 461 (0.43%)
occurrences (all)	1	4
Hypokalaemia		
subjects affected / exposed	36 / 452 (7.96%)	56 / 461 (12.15%)
occurrences (all)	78	125
Hypomagnesaemia		
subjects affected / exposed	32 / 452 (7.08%)	42 / 461 (9.11%)
occurrences (all)	59	86
Hyponatraemia		
subjects affected / exposed	3 / 452 (0.66%)	14 / 461 (3.04%)
occurrences (all)	3	23
Hypophosphataemia		
subjects affected / exposed	2 / 452 (0.44%)	2 / 461 (0.43%)
occurrences (all)	2	2
Hypoproteinaemia		
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)
occurrences (all)	0	1
Hypovolaemia		
subjects affected / exposed	2 / 452 (0.44%)	0 / 461 (0.00%)
occurrences (all)	2	0
Increased appetite		

subjects affected / exposed	1 / 452 (0.22%)	4 / 461 (0.87%)	
occurrences (all)	1	4	
Malnutrition			
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)	
occurrences (all)	0	1	
Overweight			
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)	
occurrences (all)	0	5	
Polydipsia			
subjects affected / exposed	0 / 452 (0.00%)	1 / 461 (0.22%)	
occurrences (all)	0	2	
Underweight			
subjects affected / exposed	1 / 452 (0.22%)	0 / 461 (0.00%)	
occurrences (all)	4	0	
Vitamin b12 deficiency			
subjects affected / exposed	2 / 452 (0.44%)	0 / 461 (0.00%)	
occurrences (all)	2	0	
Vitamin d deficiency			
subjects affected / exposed	2 / 452 (0.44%)	2 / 461 (0.43%)	
occurrences (all)	3	3	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
15 June 2011	<ul style="list-style-type: none">- To provide current language for the management of trebananib-related toxicities. Pleural effusion and ascites are known risks of trebananib and, thus, a new toxicity management section was added to provide guidance to participating investigators of the study.- To reword and move hypertension from exclusion to inclusion criteria.- To decrease the radiologic scanning frequency intervals, PRO collection, and CA-125 collection after 2 years on study.- To clarify that guidelines for management of hypersensitivity reactions to paclitaxel are "recommendations".- To add guidelines regarding immune modulators as excluded medications during the study.- To clarify the definition of PFS and identify the analysis sets for the primary analysis consistently with regulatory guidance documents.- To update the protocol with current language for removal of subjects and serious adverse event reporting.- To add the new pregnancy reporting section 9.4 and form (Appendix D).
24 November 2012	<ul style="list-style-type: none">- To amend Amgen documentation regarding the process for determination of expectedness of clinical trial adverse events for the purpose of expedited reporting to regulatory agencies globally.- To update with the change in timeline for serious adverse events reporting from investigators to sponsors that must now be within 24 hours.- To update the pregnancy and lactation reporting section per current Amgen protocol template. In line with this, a new lactation notification worksheet was added in Appendix D.- To clarify that this study now reports serious adverse events via electronic serious adverse event report form. A sample electronic serious adverse event contingency report form has replaced the old version in Appendix C.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported