



Clinical trial results:

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

Summary

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

Results information

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

Trial information

Trial identification

| | |
|-----------------------|----------|
| Sponsor protocol code | 20101129 |
|-----------------------|----------|

Additional study identifiers

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

Notes:

Sponsors

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

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

| | |
|--|------------------|
| Analysis stage | Final |
| Date of interim/final analysis | 05 December 2016 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 05 December 2016 |
| Was the trial ended prematurely? | Yes |

Notes:

General information about the trial

Main objective of the trial:

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

Protection of trial subjects:

This study was conducted in accordance with International Conference on Harmonisation (ICH) Good Clinical Practice (GCP) regulations/guidelines. Essential documents will be retained in accordance with ICH GCP.

All subjects provided written informed consent before undergoing any study-related procedures, including screening procedures.

The study protocol, amendments, and the informed consent form (ICF) were reviewed by the Institutional Review Boards (IRBs) and Independent Ethics Committees (IECs). No subjects were recruited into the study and no investigational product (IP) was shipped until the IRB/IEC gave written approval of the protocol and ICF and Amgen received copies of these approvals.

Background therapy: -

Evidence for comparator: -

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

Notes:

Population of trial subjects

Subjects enrolled per country

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

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

Notes:

| Subjects enrolled per age group | |
|---|-----|
| In utero | 0 |
| Preterm newborn - gestational age < 37 wk | 0 |
| Newborns (0-27 days) | 0 |
| Infants and toddlers (28 days-23 months) | 0 |
| Children (2-11 years) | 0 |
| Adolescents (12-17 years) | 0 |
| Adults (18-64 years) | 702 |
| From 65 to 84 years | 312 |
| 85 years and over | 1 |

Subject disposition

Recruitment

Recruitment details:

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

Pre-assignment

Screening details:

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

Period 1

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

Arms

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

Arm description:

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

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

Dosage and administration details:

Administered intravenously once every week

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

Dosage and administration details:

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

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

Dosage and administration details:

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

| | |
|------------------|---------------------------------------|
| Arm title | Trebananib + Paclitaxel + Carboplatin |
|------------------|---------------------------------------|

Arm description:

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

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

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

Dosage and administration details:

Trebananib 15 mg/kg administered intravenously once every week

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

Dosage and administration details:

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

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

Dosage and administration details:

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

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

Baseline characteristics

Reporting groups

| | |
|--|---------------------------------------|
| Reporting group title | Placebo + Paclitaxel + Carboplatin |
| Reporting group description: | |
| Participants received placebo intravenous (IV) infusion once a week, paclitaxel 175 mg/m ² by IV infusion once every 3 weeks (Q3W), and carboplatin at an area under the curve (AUC) 5 or 6 IV Q3W for 6 cycles followed by placebo IV once a week maintenance for 18 months. | |
| Reporting group title | Trebananib + Paclitaxel + Carboplatin |
| Reporting group description: | |
| Participants received trebananib 15 mg/kg IV once a week, paclitaxel 175 mg/m ² infusion Q3W, and carboplatin AUC 5 or 6 IV Q3W for 6 cycles followed by trebananib 15 mg/kg IV once a week maintenance for 18 months. | |

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

End points

End points reporting groups

| | |
|--|---------------------------------------|
| Reporting group title | Placebo + Paclitaxel + Carboplatin |
| Reporting group description: Participants received placebo intravenous (IV) infusion once a week, paclitaxel 175 mg/m ² by IV infusion once every 3 weeks (Q3W), and carboplatin at an area under the curve (AUC) 5 or 6 IV Q3W for 6 cycles followed by placebo IV once a week maintenance for 18 months. | |
| Reporting group title | Trebananib + Paclitaxel + Carboplatin |
| Reporting group description: Participants received trebananib 15 mg/kg IV once a week, paclitaxel 175 mg/m ² infusion Q3W, and carboplatin AUC 5 or 6 IV Q3W for 6 cycles followed by trebananib 15 mg/kg IV once a week maintenance for 18 months. | |

Primary: Progression-free Survival

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

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

Statistical analyses

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

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

Notes:

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

Secondary: Overall Survival

| | |
|--|------------------|
| End point title | Overall Survival |
| End point description: | |
| Overall survival was defined as the time from the randomization date to the date of death from any cause. Subjects who were lost to follow-up before the analysis data cutoff date or were alive by the analysis data cutoff date were censored at their last contact date (last known to be alive). "99999" indicates values that could not be estimated. | |
| End point type | Secondary |
| End point timeframe: | |
| From randomization to the data cut-off date; median overall study follow-up time was 151.3 weeks in both treatment groups. | |

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

Statistical analyses

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

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

Notes:

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

Secondary: Number of Participants with Adverse Events

| | |
|-----------------|--|
| End point title | Number of Participants with Adverse Events |
|-----------------|--|

End point description:

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

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

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

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

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

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Observed Concentration (Cmax) of Trebananib

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

End point description:

Trebananib pharmacokinetic (PK) concentrations below the lower limit of quantification of 20 ng/mL were set to 0 before data analysis. Week 7 values were based on subjects with 3 consecutive doses to ensure the steady state was reached.

The PK analysis set was defined as a subset of subjects in the safety analysis set who had evaluable concentration data.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

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

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: PK analyses were only performed in subjects in the trebananib treatment group.

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

Notes:

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

Statistical analyses

No statistical analyses for this end point

Secondary: Minimum Observed Concentration (Cmin) of Trebananib

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

End point description:

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

Week 10 Cmin values include only primary debulking surgery subjects

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Weeks 7, 10, and 19, predose

Notes:

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

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

Notes:

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

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants who Developed Anti-Trebananib Antibodies

| | |
|------------------------|---|
| End point title | Number of Participants who Developed Anti-Trebananib Antibodies |
| End point description: | Participants who developed antibody binding are defined as participants with a negative result at baseline and a positive result post-baseline. |
| End point type | Secondary |
| End point timeframe: | Day 1 of weeks 1, 10, 19, and 30 days after last dose |

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

Notes:

[7] - Subjects with a post-baseline result

[8] - Subjects with a post-baseline result

Statistical analyses

No statistical analyses for this end point

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

| | |
|-----------------|---|
| End point title | Change from Baseline in Functional Assessment of Cancer |
|-----------------|---|

End point description:

The FACT-O evaluates the health-related quality of life (HRQOL) and symptoms in patients with ovarian cancer. It consists of the FACT-G, a 27 item general cancer questionnaire and a 12-item ovarian cancer-specific subscale (OCS). Each item is scored by the participant on a scale from 0 (not at all true) to 4 (very much true). The total score ranges from 0 to 156; a higher total score indicates better quality of life or less severe symptoms.

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

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

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

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

Notes:

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

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

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

The PRO analysis set includes a subset of randomized subjects who had a baseline PRO assessment and at least one post-baseline PRO assessment prior to disease progression and the initiation of subsequent anticancer therapy.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

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

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

Notes:

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

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

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

The EQ-5D is a standardized instrument for use as a generic, preference-based measure of health outcome. The EQ-5D questionnaire captures two basic types of information, a descriptive "profile," or "health state," and an overall health rating using a visual analogue scale.

The health state includes five dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Each question has 3 answer choices: 1 (no problems), 2 (moderate problems), and 3 (extreme problems). The health states for each respondent are converted into a single index number using a specified set of weights. Resulting scores can range from 1.0 and -0.594. A higher score indicates a more preferred health status with 1.0 representing perfect health.

The PRO analysis set includes a subset of randomized subjects who had a baseline assessment and at least 1 post-baseline PRO assessment prior to disease progression and the initiation of subsequent anticancer therapy.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

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

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

Notes:

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

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

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

The EQ-5D is a standardized instrument for use as a generic, preference-based measure of health outcome. The EQ-5D questionnaire captures two basic types of information, a descriptive "profile," or "health state," and an overall health rating using a visual analogue scale (VAS).

The visual analogue scale asks respondents to rate their present health status on a 0 - 100 visual analogue scale, with 0 labeled as "Worst imaginable health state" and 100 labeled as "Best imaginable health state." The VAS score is determined by observing the point at which the subjects hand drawn line intersects the scale.

The PRO analysis set includes the subset of randomized subjects who had a baseline assessment and at least 1 post-baseline PRO assessment prior to disease progression and the initiation of subsequent anticancer therapy.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

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

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

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

Notes:

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

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

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

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

Adverse event reporting additional description:

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

| | |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|------|
| Dictionary version | 19.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|---------------------------------------|
| Reporting group title | Trebananib + Paclitaxel + Carboplatin |
|-----------------------|---------------------------------------|

Reporting group description:

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

| | |
|-----------------------|------------------------------------|
| Reporting group title | Placebo + Paclitaxel + Carboplatin |
|-----------------------|------------------------------------|

Reporting group description:

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

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

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

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

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

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

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

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

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

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

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 675 (0.15%) | 0 / 336 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Injury, poisoning and procedural complications | | | |
| Abdominal wound dehiscence | | | |
| subjects affected / exposed | 1 / 675 (0.15%) | 0 / 336 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Craniocerebral injury | | | |
| subjects affected / exposed | 1 / 675 (0.15%) | 0 / 336 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Femoral neck fracture | | | |
| subjects affected / exposed | 1 / 675 (0.15%) | 0 / 336 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Femur fracture | | | |
| subjects affected / exposed | 1 / 675 (0.15%) | 0 / 336 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Fibula fracture | | | |
| subjects affected / exposed | 1 / 675 (0.15%) | 0 / 336 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal anastomotic leak | | | |
| subjects affected / exposed | 1 / 675 (0.15%) | 0 / 336 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hip fracture | | | |
| subjects affected / exposed | 0 / 675 (0.00%) | 1 / 336 (0.30%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Humerus fracture | | | |

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|------------------|---|
| 27 November 2012 | <ul style="list-style-type: none">- Amgen documentation regarding the process for determination of expectedness of adverse events for expedited reporting to regulatory agencies globally was amended- The timeline for serious adverse event reporting was changed (within 24 hours)- The Pregnancy and Lactation Reporting section was updated- The reporting of serious adverse events using the electronic serious adverse event report form was clarified |
| 17 January 2014 | <ul style="list-style-type: none">- The sample size was reduced from 2000 to 1000 subjects to enhance the feasibility of study completion without compromising the integrity of the primary endpoint of the study- Language on safety data collection, recording, and reporting was updated- Language on how to address and report serious adverse events occurring outside the protocol reporting period was added |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported