



Clinical trial results:

A Phase 3, Randomized, Double-Blind, Placebo-Controlled Study of Ramucirumab plus Docetaxel versus Placebo plus Docetaxel in Patients with Locally Advanced or Unresectable or Metastatic Urothelial Carcinoma Who Progressed on or after Platinum-Based Therapy.

Summary

| | |
|--------------------------|-------------------------------|
| EudraCT number | 2014-003655-66 |
| Trial protocol | ES HU DK DE NL PL GB BE GR IT |
| Global end of trial date | 26 July 2022 |

Results information

| | |
|--------------------------------|----------------|
| Result version number | v1 (current) |
| This version publication date | 09 August 2023 |
| First version publication date | 09 August 2023 |

Trial information

Trial identification

| | |
|-----------------------|-------------|
| Sponsor protocol code | I4T-MC-JVDC |
|-----------------------|-------------|

Additional study identifiers

| | |
|------------------------------------|---------------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02426125 |
| WHO universal trial number (UTN) | - |
| Other trial identifiers | Trial Number: 15679 |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Eli Lilly and Company |
| Sponsor organisation address | Lilly Corporate Center, Indianapolis, IN, United States, 46285 |
| Public contact | Available Mon - Fri 9 AM - 5 PM EST, Eli Lilly and Company, 1 877CTLilly, |
| Scientific contact | Available Mon - Fri 9 AM - 5 PM EST, Eli Lilly and Company, 1 8772854559, |

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 | 26 July 2022 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 26 July 2022 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The main purpose of this study is to evaluate the safety and efficacy of the study drug ramucirumab in combination with docetaxel in participants with urothelial cancer who failed prior platinum-based therapy.

Protection of trial subjects:

This study was conducted in accordance with International Conference on Harmonization (ICH) Good Clinical Practice, and the principles of the Declaration of Helsinki, in addition to following the laws and regulations of the country or countries in which a study is conducted.

Background therapy: -

Evidence for comparator: -

| | |
|---|--------------|
| Actual start date of recruitment | 13 July 2015 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|------------------------|
| Country: Number of subjects enrolled | Romania: 10 |
| Country: Number of subjects enrolled | Hungary: 13 |
| Country: Number of subjects enrolled | United States: 35 |
| Country: Number of subjects enrolled | Japan: 54 |
| Country: Number of subjects enrolled | Ukraine: 8 |
| Country: Number of subjects enrolled | United Kingdom: 42 |
| Country: Number of subjects enrolled | Russian Federation: 30 |
| Country: Number of subjects enrolled | Spain: 37 |
| Country: Number of subjects enrolled | Greece: 26 |
| Country: Number of subjects enrolled | Canada: 9 |
| Country: Number of subjects enrolled | Korea, Republic of: 25 |
| Country: Number of subjects enrolled | Netherlands: 35 |
| Country: Number of subjects enrolled | Turkey: 28 |
| Country: Number of subjects enrolled | Belgium: 7 |
| Country: Number of subjects enrolled | Taiwan: 31 |
| Country: Number of subjects enrolled | Denmark: 11 |
| Country: Number of subjects enrolled | Poland: 8 |
| Country: Number of subjects enrolled | Italy: 37 |
| Country: Number of subjects enrolled | Mexico: 4 |

| | |
|--------------------------------------|---------------|
| Country: Number of subjects enrolled | Israel: 18 |
| Country: Number of subjects enrolled | Australia: 12 |
| Country: Number of subjects enrolled | France: 34 |
| Country: Number of subjects enrolled | Germany: 16 |
| Worldwide total number of subjects | 530 |
| EEA total number of subjects | 234 |

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) | 239 |
| From 65 to 84 years | 289 |
| 85 years and over | 2 |

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Completers include participants who are confirmed to be alive at study completion.

Period 1

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

Arms

| | |
|------------------------------|-----|
| Are arms mutually exclusive? | Yes |
|------------------------------|-----|

| | |
|------------------|-------------------------|
| Arm title | Ramucirumab + Docetaxel |
|------------------|-------------------------|

Arm description:

Ramucirumab (10 milligram/kilogram [mg/kg]) intravenously (IV) plus docetaxel (75 milligram/square meter [mg/m²]) IV on day 1 of each 21-day cycle. Participants may continue to receive treatment until discontinuation criteria are met.

| | |
|--|-----------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Ramucirumab |
| Investigational medicinal product code | |
| Other name | LY3009806 |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Participants received 10 mg/kg of Ramucirumab intravenously (IV) on day 1 of each 21-day cycle.

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

Dosage and administration details:

Participants received 75 mg/m² of docetaxel Intravenously on day 1 of each 21-day cycle.

| | |
|------------------|---------------------|
| Arm title | Placebo + Docetaxel |
|------------------|---------------------|

Arm description:

Placebo IV plus docetaxel (75 mg/m²) IV on day 1 of each 21-day cycle. Participants may continue to receive treatment until discontinuation criteria are met.

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

Dosage and administration details:

Participants received 75 mg/m² of docetaxel intravenously on day 1 of each 21-day cycle.

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

Dosage and administration details:

Participants received matching placebo intravenously on day 1 of each 21-day cycle.

| Number of subjects in period 1 | Ramucirumab + Docetaxel | Placebo + Docetaxel |
|--|----------------------------|---------------------|
| Started | 263 | 267 |
| Received at least one dose of study drug | 258 | 265 |
| Completed | 46 | 39 |
| Not completed | 217 | 228 |
| Adverse event, serious fatal | 185 | 200 |
| Consent withdrawn by subject | 13 | 14 |
| Randomized, But Never Treated | 5 | 2 |
| Lost to follow-up | 14 | 12 |

Baseline characteristics

Reporting groups

| | |
|-----------------------|-------------------------|
| Reporting group title | Ramucirumab + Docetaxel |
|-----------------------|-------------------------|

Reporting group description:

Ramucirumab (10 milligram/kilogram [mg/kg]) intravenously (IV) plus docetaxel (75 milligram/square meter [mg/m²]) IV on day 1 of each 21-day cycle. Participants may continue to receive treatment until discontinuation criteria are met.

| | |
|-----------------------|---------------------|
| Reporting group title | Placebo + Docetaxel |
|-----------------------|---------------------|

Reporting group description:

Placebo IV plus docetaxel (75 mg/m²) IV on day 1 of each 21-day cycle. Participants may continue to receive treatment until discontinuation criteria are met.

| Reporting group values | Ramucirumab + Docetaxel | Placebo + Docetaxel | Total |
|------------------------------------|-------------------------|---------------------|-------|
| Number of subjects | 263 | 267 | 530 |
| Age categorical Units: Subjects | | | |

| | | | |
|---|---------------|---------------|-----|
| Age continuous Units: years arithmetic mean standard deviation | 64.6 ± 9.9 | 64.8 ± 9.2 | - |
| Gender categorical Units: Subjects | | | |
| Female | 50 | 52 | 102 |
| Male | 213 | 215 | 428 |
| Ethnicity (NIH/OMB) Units: Subjects | | | |
| Hispanic or Latino | 13 | 10 | 23 |
| Not Hispanic or Latino | 208 | 219 | 427 |
| Unknown or Not Reported | 42 | 38 | 80 |
| Race (NIH/OMB) Units: Subjects | | | |
| American Indian or Alaska Native | 1 | 0 | 1 |
| Asian | 54 | 61 | 115 |
| Native Hawaiian or Other Pacific Islander | 0 | 0 | 0 |
| Black or African American | 3 | 2 | 5 |
| White | 203 | 204 | 407 |
| More than one race | 0 | 0 | 0 |
| Unknown or Not Reported | 2 | 0 | 2 |
| Region of Enrollment Units: Subjects | | | |
| Romania | 5 | 5 | 10 |
| Hungary | 5 | 8 | 13 |
| United States | 17 | 18 | 35 |
| Japan | 24 | 30 | 54 |
| Ukraine | 5 | 3 | 8 |
| United Kingdom | 18 | 24 | 42 |

| | | | |
|-------------|----|----|----|
| Russia | 18 | 12 | 30 |
| Spain | 22 | 15 | 37 |
| Greece | 13 | 13 | 26 |
| Canada | 4 | 5 | 9 |
| South Korea | 16 | 9 | 25 |
| Netherlands | 17 | 18 | 35 |
| Turkey | 11 | 17 | 28 |
| Belgium | 6 | 1 | 7 |
| Taiwan | 13 | 18 | 31 |
| Denmark | 5 | 6 | 11 |
| Poland | 4 | 4 | 8 |
| Italy | 23 | 14 | 37 |
| Mexico | 3 | 1 | 4 |
| Israel | 7 | 11 | 18 |
| Australia | 6 | 6 | 12 |
| France | 16 | 18 | 34 |
| Germany | 5 | 11 | 16 |

End points

End points reporting groups

| | |
|---|-------------------------|
| Reporting group title | Ramucirumab + Docetaxel |
| Reporting group description: Ramucirumab (10 milligram/kilogram [mg/kg]) intravenously (IV) plus docetaxel (75 milligram/square meter [mg/m ²]) IV on day 1 of each 21-day cycle. Participants may continue to receive treatment until discontinuation criteria are met. | |
| Reporting group title | Placebo + Docetaxel |
| Reporting group description: Placebo IV plus docetaxel (75 mg/m ²) IV on day 1 of each 21-day cycle. Participants may continue to receive treatment until discontinuation criteria are met. | |

Primary: Progression Free Survival (PFS)

| | |
|--|---------------------------------|
| End point title | Progression Free Survival (PFS) |
| End point description: PFS defined as time from first day of therapy to first evidence of disease progression defined by Response Evaluation Criteria in Solid Tumors (RECIST v1.1) or death from any cause. Progressive Disease (PD) is at least 20% increase in sum of diameters of target lesions, with reference being the smallest sum on study and plus absolute increase of at least 5 mm, or unequivocal progression of non-target lesions, or 1 or more new lesions. If participant does not have complete baseline disease assessment, then PFS time was censored at date of first dose, regardless of whether or not objectively determined disease progression or death has been observed for participant. If participant is not known to have died or have objective progression as of data inclusion cutoff date for analysis, PFS time was censored at last adequate tumor assessment date. Analysis population description (APD): All randomized participants. Censored participants: Ramucirumab + Docetaxel = 51, Placebo + Docetaxel = 31. | |
| End point type | Primary |
| End point timeframe: Randomization to Radiological Disease Progression or Death from Any Cause (Up to 29.7 Months) | |

| End point values | Ramucirumab + Docetaxel | Placebo + Docetaxel | | |
|----------------------------------|-------------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 263 | 267 | | |
| Units: Months | | | | |
| median (confidence interval 95%) | 4.07 (3.29 to 4.83) | 2.76 (2.60 to 2.89) | | |

Statistical analyses

| | |
|----------------------------|---|
| Statistical analysis title | Progression Free Survival (PFS) |
| Comparison groups | Ramucirumab + Docetaxel v Placebo + Docetaxel |

| | |
|---|-------------------------|
| Number of subjects included in analysis | 530 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0002 ^[1] |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.696 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.573 |
| upper limit | 0.845 |

Notes:

[1] - Stratified

Secondary: Overall Survival (OS)

| | |
|--|-----------------------|
| End point title | Overall Survival (OS) |
| End point description: | |
| OS is the time from the date of randomization to the date of death from any cause. For each participant who is not known to have died as of the data inclusion cutoff date for a particular analysis, OS was censored for that analysis at the last known alive date prior to the data inclusion cutoff date. APD: All randomized participants. Censored participants: Ramucirumab + Docetaxel = 78, Placebo + Docetaxel = 67. | |
| End point type | Secondary |
| End point timeframe: | |
| Randomization to Date of Death from Any Cause (Up to 31.1 Months) | |

| End point values | Ramucirumab + Docetaxel | Placebo + Docetaxel | | |
|----------------------------------|-------------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 263 | 267 | | |
| Units: Months | | | | |
| median (confidence interval 95%) | 9.40 (7.89 to 11.43) | 7.85 (7.00 to 9.30) | | |

Statistical analyses

| | |
|---|---|
| Statistical analysis title | Overall Survival (OS) |
| Comparison groups | Ramucirumab + Docetaxel v Placebo + Docetaxel |
| Number of subjects included in analysis | 530 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.2461 ^[2] |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.887 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.724 |
| upper limit | 1.086 |

Notes:

[2] - Stratified

Secondary: Percentage of Participants with an Objective Response Rate (ORR)

| | |
|-----------------|--|
| End point title | Percentage of Participants with an Objective Response Rate (ORR) |
|-----------------|--|

End point description:

ORR is defined as the percentage of participants who achieve a best overall response of complete response (CR) + partial response (PR). ORR = CR + PR. CR is defined as disappearance of all target and non-target lesions. Any pathological lymph nodes (whether target or nontarget) must have reduction in short axis to < 10 millimeter (mm). Tumor-marker results must have normalized. PR is at least a 30% decrease in the sum of diameters of target lesions, taking as reference the baseline sum diameters. Best overall response is classified based on the overall responses assessed by study investigators according to RECIST v1.1. APD: All randomized participants.

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

End point timeframe:

Randomization to Disease Progression (Up to 29.7 Months)

| End point values | Ramucirumab + Docetaxel | Placebo + Docetaxel | | |
|-----------------------------------|-------------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 263 | 267 | | |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | 25.9 (20.6 to 31.1) | 13.9 (9.7 to 18.0) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Disease Control Rate (DCR)

| | |
|-----------------|--|
| End point title | Percentage of Participants with Disease Control Rate (DCR) |
|-----------------|--|

End point description:

DCR is percentage of participants with a best overall response of CR, PR, or Stable Disease (SD) as per Response using RECIST v1.1. Target lesions - CR: Disappearance of all lesions; any pathological lymph nodes must have reduction in short axis to <10 mm. PR: At least a 30% decrease in sum of diameters of lesions vs baseline sum. Progressive Disease (PD): At least a 20% increase in sum of diameters of lesions vs smallest sum on study (the sum must also demonstrate an absolute increase of at least 5 mm); or the appearance of new lesion(s). SD: Neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for PD. Non target lesions - CR: Disappearance of all lesions and normalization of tumor marker levels; all lymph nodes must be non-pathological in size. Non-CR/Non-PD: Persistence of lesion(s) and/or maintenance of abnormal tumor marker levels. PD: Unequivocal progression of existing lesions or the appearance of new lesion(s). APD: All randomized participants.

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

End point timeframe:

Randomization to Disease Progression (Up to 29.7 Months)

| End point values | Ramucirumab + Docetaxel | Placebo + Docetaxel | | |
|-----------------------------------|-------------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 263 | 267 | | |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | 65.4 (59.7 to 71.1) | 55.1 (49.1 to 61.0) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (DoR)

| | |
|---|----------------------------|
| End point title | Duration of Response (DoR) |
| End point description: | |
| Objective response was achieved if they had a best overall response of CR or PR. Target lesions- CR: Disappearance of all lesions;any pathological lymph nodes have reduction in short axis to <10 mm.PR: At least a 30% decrease in sum of diameters of lesions vs the baseline sum.PD: At least a 20% increase in sum of diameters of lesions vs smallest sum on study(the sum must also demonstrate an absolute increase of at least 5 mm); or appearance of new lesion(s). Non target lesions - CR: Disappearance of all lesions and normalization of tumour marker levels; all lymph nodes must be non-pathological in size. Non-CR/Non-PD: Persistence of lesion(s) and/or maintenance of abnormal tumor marker levels. PD: Unequivocal progression of existing lesions or appearance of new lesion(s). If a participant was not known to have died or have radiographically documented PD as of data inclusion cutoff date, DOR was censored at the date of the last adequate tumor assessment. APD: All randomized participants | |
| End point type | Secondary |
| End point timeframe: | |
| Date of Complete Response (CR) or Partial Response (PR) to Date of Objective Disease Progression or Death Due to Any Cause (Up to 28.4 Months) | |
| Participants censored in Ramucirumab + Docetaxel = 12 and in Placebo + Docetaxel = 5. | |

| End point values | Ramucirumab + Docetaxel | Placebo + Docetaxel | | |
|----------------------------------|-------------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 68 | 37 | | |
| Units: Months | | | | |
| median (confidence interval 95%) | 5.32 (3.94 to 6.87) | 4.17 (3.29 to 5.55) | | |

Statistical analyses

| | |
|----------------------------|---|
| Statistical analysis title | Duration of Response (DoR) |
| Comparison groups | Ramucirumab + Docetaxel v Placebo + Docetaxel |

| | |
|---|-------------------|
| Number of subjects included in analysis | 105 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.189 |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.74 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.473 |
| upper limit | 1.158 |

Secondary: Time to Deterioration in Quality of Life (QoL) on the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30 (EORTC QLQ-C30) - Global Health Status/ QoL Scale

| | |
|-----------------|--|
| End point title | Time to Deterioration in Quality of Life (QoL) on the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30 (EORTC QLQ-C30) - Global Health Status/ QoL Scale |
|-----------------|--|

End point description:

Time to sustained deterioration was defined as time from randomization to first worsening in QoL with no subsequent non-worsened assessment. Worsening in global health status/QoL was defined as a decrease of ≥ 10 points on a 100-point scale. If a participant did not report worsening, time to sustained deterioration was censored at date of last non-worsened assessment. Scores for global health status/QoL range from 0 to 100 with; higher scores representing better QoL. APD: All randomized participants. Censored participants: Ramucirumab + Docetaxel = 160, Placebo + Docetaxel = 173.

| | |
|--|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Randomization, 30 Days After Treatment Discontinuation (Up to 18 Months) | |

| End point values | Ramucirumab + Docetaxel | Placebo + Docetaxel | | |
|----------------------------------|-------------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 263 | 267 | | |
| Units: Months | | | | |
| median (confidence interval 95%) | 6.87 (4.24 to 8.90) | 4.60 (3.52 to 5.55) | | |

Statistical analyses

| | |
|----------------------------|---|
| Statistical analysis title | Global health status/QoL |
| Comparison groups | Ramucirumab + Docetaxel v Placebo + Docetaxel |

| | |
|---|----------------------------|
| Number of subjects included in analysis | 530 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[3] |
| P-value | = 0.357 ^[4] |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.879 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.663 |
| upper limit | 1.167 |

Notes:

[3] - Global health status/QoL

[4] - Stratified

Secondary: Change from Baseline on the EuroQol 5-Dimension, 5-Level Questionnaire (EQ-5D-5L) Index Score

| | |
|-----------------|---|
| End point title | Change from Baseline on the EuroQol 5-Dimension, 5-Level Questionnaire (EQ-5D-5L) Index Score |
|-----------------|---|

End point description:

The EQ-5D-5L is a standardized instrument for use as a measure of self-reported health status. Participants completed the 5-level (no problem, slight problem, moderate problem, severe problem, and inability or extreme problem), 5-dimension (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression) questionnaire concerning their current health state. A unique EQ-5D health state is defined by combining 1 level from each of the 5 dimensions. Scores range from 0 (death) to 1 (perfect health), but scores <0 are possible based on the algorithm. APD: All randomized participants with baseline and 30-day follow-up data.

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

End point timeframe:

Randomization, 30 Days After Treatment Discontinuation (Up to 18 Months)

| End point values | Ramucirumab + Docetaxel | Placebo + Docetaxel | | |
|--------------------------------------|-------------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 83 | 102 | | |
| Units: units on a scale | | | | |
| arithmetic mean (standard deviation) | -0.10 (± 0.26) | -0.19 (± 0.26) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline on the EuroQol 5-Dimension, 5-Level Questionnaire (EQ-5D-5L) Visual Analogue Scale (VAS)

| | |
|-----------------|---|
| End point title | Change from Baseline on the EuroQol 5-Dimension, 5-Level Questionnaire (EQ-5D-5L) Visual Analogue Scale (VAS) |
|-----------------|---|

End point description:

The EQ-5D-5L is a standardized instrument for use as a measure of self-reported health status. A unique

EQ-5D health state is defined by combining 1 level from each of the 5 dimensions. Participants indicated their current health status by marking on a VAS ranging from 100 (best imaginable health state) to 0 (worst imaginable health state).

APD: All randomized participants with baseline and 30-day follow-up data.

| | |
|--|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Randomization, 30 Days After Treatment Discontinuation (Up to 18 Months) | |

| End point values | Ramucirumab + Docetaxel | Placebo + Docetaxel | | |
|--------------------------------------|-------------------------|-----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 86 | 105 | | |
| Units: millimeter (mm) | | | | |
| arithmetic mean (standard deviation) | -7.87 (\pm 17.95) | -10.91 (\pm 16.77) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetics (PK): Maximum Concentration (Cmax) of Ramucirumab

| | |
|-----------------|---|
| End point title | Pharmacokinetics (PK): Maximum Concentration (Cmax) of Ramucirumab ^[5] |
|-----------------|---|

End point description:

Cmax of Ramucirumab at the end of ramucirumab infusion. APD: All randomized participants who had evaluable PK data.

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

End point timeframe:

Cycle 1 and Cycle 9, Day 1: Predose, Postdose

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: The endpoint is planned only for Ramucirumab arm in the baseline period per protocol.

| End point values | Ramucirumab + Docetaxel | | | |
|---|-------------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 209 ^[6] | | | |
| Units: microgram/milliliter (μ g/mL) | | | | |
| geometric mean (geometric coefficient of variation) | | | | |
| Cycle 1 | 199 (\pm 28) | | | |
| Cycle 9 | 265 (\pm 29) | | | |

Notes:

[6] - Cycle 1: 209

Cycle 9: 22

Statistical analyses

No statistical analyses for this end point

Secondary: PK: Minimum Concentration (Cmin) of Ramucirumab

| | |
|-----------------|--|
| End point title | PK: Minimum Concentration (Cmin) of Ramucirumab ^[7] |
|-----------------|--|

End point description:

Cmin of Ramucirumab following administration every 3 weeks. APD: All randomized participants who had evaluable PK data.

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

End point timeframe:

Day 1 of Cycle 2, 3, 5 and 9 (Predose and Postdose)

Notes:

[7] - 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: The endpoint is planned only for Ramucirumab arm in the baseline period per protocol.

| End point values | Ramucirumab + Docetaxel | | | |
|---|-------------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 188 ^[8] | | | |
| Units: µg/mL | | | | |
| geometric mean (geometric coefficient of variation) | | | | |
| Cycle 2 | 14.9 (± 64) | | | |
| Cycle 3 | 23.5 (± 63) | | | |
| Cycle 5 | 32.5 (± 70) | | | |
| Cycle 9 | 48.9 (± 56) | | | |

Notes:

[8] - Cycle 2: 188; Cycle 3: 146; Cycle 5: 94; Cycle 9: 25

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Anti-Ramucirumab Antibodies

| | |
|-----------------|---|
| End point title | Number of Participants with Anti-Ramucirumab Antibodies |
|-----------------|---|

End point description:

Number of participants with positive treatment emergent anti-ramucirumab antibodies was summarized by treatment group. APD: All randomized participants who received at least one dose of study drug at baseline and post-baseline.

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

End point timeframe:

29.7 Months

| | | | | |
|-----------------------------|-------------------------|---------------------|--|--|
| End point values | Ramucirumab + Docetaxel | Placebo + Docetaxel | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 199 | 213 | | |
| Units: participants | 3 | 8 | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 64.7 Months

Adverse event reporting additional description:

All randomized participants who received at least one dose of study drug. Gender specific events only occurring in male or female participants have had the number of participants At Risk adjusted accordingly.

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 26.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|-------------------|
| Reporting group title | Placebo+Docetaxel |
|-----------------------|-------------------|

Reporting group description:

Placebo IV plus docetaxel (75 mg/m²) IV on day 1 of each 21-day cycle. Participants may continue to receive treatment until discontinuation criteria are met.

| | |
|-----------------------|-------------------------|
| Reporting group title | Ramucirumab + Docetaxel |
|-----------------------|-------------------------|

Reporting group description:

Ramucirumab (10 mg/kg) IV plus docetaxel (75 mg/m²) IV on day 1 of each 21-day cycle. Participants may continue to receive treatment until discontinuation criteria are met.

| Serious adverse events | Placebo+Docetaxel | Ramucirumab + Docetaxel | |
|---|--------------------|-------------------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 107 / 265 (40.38%) | 111 / 258 (43.02%) | |
| number of deaths (all causes) | 209 | 193 | |
| number of deaths resulting from adverse events | 5 | 8 | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| tumour haemorrhage | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vascular disorders | | | |
| arterial haemorrhage | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|--|-----------------|-----------------|--|
| aortic aneurysm | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deep vein thrombosis | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 2 / 265 (0.75%) | 2 / 258 (0.78%) | |
| occurrences causally related to treatment / all | 0 / 2 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| embolism | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 1 / 258 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| haematoma | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| hypertension | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 2 / 258 (0.78%) | |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| hypotension | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| venous occlusion | | | |
| alternative dictionary used: MedDRA 26.0 | | | |

| | | | |
|--|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General disorders and administration site conditions | | | |
| asthenia | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 2 / 265 (0.75%) | 0 / 258 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 1 / 1 | 0 / 0 | |
| chest pain | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| death | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 2 / 265 (0.75%) | 2 / 258 (0.78%) | |
| occurrences causally related to treatment / all | 1 / 2 | 1 / 2 | |
| deaths causally related to treatment / all | 1 / 2 | 1 / 2 | |
| fatigue | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 2 / 265 (0.75%) | 5 / 258 (1.94%) | |
| occurrences causally related to treatment / all | 2 / 2 | 3 / 5 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| general physical health deterioration | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| generalised oedema | | | |
| alternative dictionary used: MedDRA 26.0 | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| malaise | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 1 / 258 (0.39%) | |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| mucosal inflammation | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 1 / 258 (0.39%) | |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| non-cardiac chest pain | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 2 / 258 (0.78%) | |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| pain | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 2 / 265 (0.75%) | 0 / 258 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| pyrexia | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 9 / 265 (3.40%) | 3 / 258 (1.16%) | |
| occurrences causally related to treatment / all | 2 / 10 | 2 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| sudden death | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |

| | | | |
|---|-----------------|-----------------|--|
| Reproductive system and breast disorders | | | |
| female genital tract fistula | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed ^[1] | 0 / 265 (0.00%) | 1 / 49 (2.04%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| chronic obstructive pulmonary disease | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| dyspnoea | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 3 / 265 (1.13%) | 3 / 258 (1.16%) | |
| occurrences causally related to treatment / all | 1 / 3 | 3 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| epistaxis | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| hiccups | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| laryngeal inflammation | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|--|-----------------|-----------------|--|
| obstructive airways disorder alternative dictionary used: MedDRA 26.0 subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| pleural effusion alternative dictionary used: MedDRA 26.0 subjects affected / exposed | 7 / 265 (2.64%) | 0 / 258 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 8 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| pneumonitis alternative dictionary used: MedDRA 26.0 subjects affected / exposed | 1 / 265 (0.38%) | 2 / 258 (0.78%) | |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 2 | |
| deaths causally related to treatment / all | 1 / 1 | 0 / 1 | |
| pneumothorax alternative dictionary used: MedDRA 26.0 subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| pulmonary embolism alternative dictionary used: MedDRA 26.0 subjects affected / exposed | 2 / 265 (0.75%) | 1 / 258 (0.39%) | |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 1 / 1 | 0 / 0 | |
| pulmonary hypertension alternative dictionary used: MedDRA 26.0 subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Psychiatric disorders delirium alternative dictionary used: MedDRA 26.0 | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 2 / 265 (0.75%) | 0 / 258 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| mental status changes | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Product issues | | | |
| device connection issue | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Investigations | | | |
| blood creatinine increased | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 2 / 265 (0.75%) | 1 / 258 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| neutrophil count decreased | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 2 / 265 (0.75%) | 2 / 258 (0.78%) | |
| occurrences causally related to treatment / all | 3 / 3 | 3 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| platelet count decreased | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 2 / 258 (0.78%) | |
| occurrences causally related to treatment / all | 0 / 1 | 2 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Injury, poisoning and procedural complications | | | |
| fall | | | |
| alternative dictionary used: MedDRA 26.0 | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 265 (0.38%) | 1 / 258 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| infusion related reaction | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 2 / 258 (0.78%) | |
| occurrences causally related to treatment / all | 1 / 1 | 2 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| lower limb fracture | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| urostomy complication | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac disorders | | | |
| arteriospasm coronary | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| cardiac arrest | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 1 / 1 | |
| cardiac failure | | | |
| alternative dictionary used: MedDRA 26.0 | | | |

| | | | |
|--|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 265 (0.38%) | 1 / 258 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| cardiac failure congestive alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 1 / 258 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| intracardiac thrombus alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| myocardial infarction alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 2 / 258 (0.78%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| pericardial effusion alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| supraventricular tachycardia alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nervous system disorders basilar artery thrombosis alternative dictionary used: MedDRA 26.0 | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 1 / 1 | |
| cerebrovascular accident alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 1 / 258 (0.39%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| cerebral ischaemia alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| dizziness alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| headache alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| presyncope alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| subarachnoid haemorrhage alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|--------------------------------------|--------------------------------------|--|
| syncope alternative dictionary used: MedDRA 26.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 2 / 265 (0.75%) 0 / 2 0 / 0 | 1 / 258 (0.39%) 0 / 1 0 / 0 | |
| transient ischaemic attack alternative dictionary used: MedDRA 26.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 265 (0.38%) 1 / 1 0 / 0 | 0 / 258 (0.00%) 0 / 0 0 / 0 | |
| Blood and lymphatic system disorders | | | |
| anaemia alternative dictionary used: MedDRA 26.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 4 / 265 (1.51%) 1 / 4 0 / 0 | 0 / 258 (0.00%) 0 / 0 0 / 0 | |
| blood loss anaemia alternative dictionary used: MedDRA 26.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 265 (0.00%) 0 / 0 0 / 0 | 1 / 258 (0.39%) 0 / 1 0 / 0 | |
| febrile neutropenia alternative dictionary used: MedDRA 26.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 13 / 265 (4.91%) 11 / 14 0 / 0 | 17 / 258 (6.59%) 20 / 20 0 / 0 | |
| leukopenia alternative dictionary used: MedDRA 26.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 2 / 265 (0.75%) 3 / 3 0 / 0 | 0 / 258 (0.00%) 0 / 0 0 / 0 | |
| neutropenia alternative dictionary used: MedDRA 26.0 | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 2 / 265 (0.75%) | 4 / 258 (1.55%) | |
| occurrences causally related to treatment / all | 2 / 2 | 5 / 5 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| pancytopenia | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ear and labyrinth disorders | | | |
| vertigo | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| abdominal pain | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 1 / 258 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 1 | 2 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| anal fistula | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 1 / 258 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| ascites | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| constipation | | | |
| alternative dictionary used: MedDRA 26.0 | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| colitis | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 1 / 258 (0.39%) | |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| gastric haemorrhage | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 1 / 1 | |
| diarrhoea | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 4 / 265 (1.51%) | 6 / 258 (2.33%) | |
| occurrences causally related to treatment / all | 3 / 5 | 5 / 6 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| fistula of small intestine | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| enterovesical fistula | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 1 / 1 | |
| enterocolitis | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|--|-----------------|-----------------|--|
| gastrointestinal haemorrhage | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 2 / 258 (0.78%) | |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| gastrointestinal ulcer | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| haemorrhoids | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| ileal perforation | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| intestinal ischaemia | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| intestinal obstruction | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 2 / 265 (0.75%) | 3 / 258 (1.16%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| intestinal perforation | | | |
| alternative dictionary used: MedDRA 26.0 | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| large intestine perforation alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 2 / 258 (0.78%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| oesophagitis alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| nausea alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 2 / 265 (0.75%) | 2 / 258 (0.78%) | |
| occurrences causally related to treatment / all | 1 / 2 | 2 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| tooth disorder alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| rectal haemorrhage alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| small intestinal obstruction alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|--|-----------------------------------|-----------------------------------|--|
| small intestinal perforation alternative dictionary used: MedDRA 26.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 265 (0.00%) 0 / 0 0 / 0 | 1 / 258 (0.39%) 1 / 1 0 / 0 | |
| stomatitis alternative dictionary used: MedDRA 26.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 265 (0.38%) 0 / 1 0 / 0 | 0 / 258 (0.00%) 0 / 0 0 / 0 | |
| upper gastrointestinal haemorrhage alternative dictionary used: MedDRA 26.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 265 (0.38%) 1 / 1 0 / 0 | 0 / 258 (0.00%) 0 / 0 0 / 0 | |
| vomiting alternative dictionary used: MedDRA 26.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 2 / 265 (0.75%) 2 / 2 0 / 0 | 3 / 258 (1.16%) 3 / 3 0 / 0 | |
| Hepatobiliary disorders cholelithiasis alternative dictionary used: MedDRA 26.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 265 (0.00%) 0 / 0 0 / 0 | 1 / 258 (0.39%) 0 / 1 0 / 0 | |
| Skin and subcutaneous tissue disorders dermatitis alternative dictionary used: MedDRA 26.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all rash alternative dictionary used: MedDRA 26.0 | 1 / 265 (0.38%) 1 / 1 0 / 0 | 0 / 258 (0.00%) 0 / 0 0 / 0 | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal and urinary disorders | | | |
| acute kidney injury | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 3 / 258 (1.16%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| haematuria | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 6 / 265 (2.26%) | 4 / 258 (1.55%) | |
| occurrences causally related to treatment / all | 1 / 6 | 1 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| hydronephrosis | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| renal failure | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 3 / 258 (1.16%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 1 / 2 | |
| ureteric stenosis | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (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 | | | |
| alternative dictionary used: MedDRA 26.0 | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 265 (0.38%) | 2 / 258 (0.78%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Endocrine disorders | | | |
| adrenal insufficiency | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal and connective tissue disorders | | | |
| back pain | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 2 / 265 (0.75%) | 1 / 258 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| bone pain | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| fistula | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| myalgia | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| muscular weakness | | | |
| alternative dictionary used: MedDRA 26.0 | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| abdominal abscess | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| appendicitis | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| bronchitis | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| bacteraemia | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| cellulitis | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| cystitis | | | |
| alternative dictionary used: MedDRA 26.0 | | | |

| | | | |
|--|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 265 (0.38%) | 1 / 258 (0.39%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| clostridium difficile colitis alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| diverticulitis alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| device related infection alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 3 / 258 (1.16%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| gastroenteritis alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 1 / 258 (0.39%) | |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| gingivitis alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| kidney infection alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (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 alternative dictionary used: MedDRA 26.0 | | | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) | | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | | |
| infection alternative dictionary used: MedDRA 26.0 | | | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 1 / 258 (0.39%) | | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | | |
| neutropenic sepsis alternative dictionary used: MedDRA 26.0 | | | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) | | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | 1 / 1 | | |
| pneumonia alternative dictionary used: MedDRA 26.0 | | | | |
| subjects affected / exposed | 8 / 265 (3.02%) | 5 / 258 (1.94%) | | |
| occurrences causally related to treatment / all | 3 / 8 | 3 / 5 | | |
| deaths causally related to treatment / all | 1 / 3 | 0 / 0 | | |
| pneumonia aspiration alternative dictionary used: MedDRA 26.0 | | | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 1 / 258 (0.39%) | | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | | |
| pyelonephritis alternative dictionary used: MedDRA 26.0 | | | | |
| subjects affected / exposed | 2 / 265 (0.75%) | 2 / 258 (0.78%) | | |
| occurrences causally related to treatment / all | 1 / 2 | 1 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | | |
| respiratory tract infection alternative dictionary used: MedDRA 26.0 | | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| sepsis | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 5 / 265 (1.89%) | 7 / 258 (2.71%) | |
| occurrences causally related to treatment / all | 5 / 5 | 3 / 7 | |
| deaths causally related to treatment / all | 0 / 0 | 1 / 4 | |
| stoma site abscess | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| toxic shock syndrome | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| urosepsis | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 5 / 265 (1.89%) | 2 / 258 (0.78%) | |
| occurrences causally related to treatment / all | 3 / 5 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| urinary tract infection | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 11 / 265 (4.15%) | 10 / 258 (3.88%) | |
| occurrences causally related to treatment / all | 2 / 15 | 2 / 11 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metabolism and nutrition disorders | | | |
| dehydration | | | |
| alternative dictionary used: MedDRA 26.0 | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| decreased appetite | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) | |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| diabetic metabolic decompensation | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| hyperglycaemia | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 1 / 258 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| hyperkalaemia | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 2 / 258 (0.78%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| hyponatraemia | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 3 / 258 (1.16%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.

Justification: Gender specific events only occurring in male or female participants have had the number of participants At Risk adjusted accordingly.

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

| Non-serious adverse events | Placebo+Docetaxel | Ramucirumab + Docetaxel | |
|---|--------------------|-------------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 251 / 265 (94.72%) | 241 / 258 (93.41%) | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| neuroma | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) | |
| occurrences (all) | 0 | 1 | |
| pyogenic granuloma | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) | |
| occurrences (all) | 0 | 1 | |
| tumour necrosis | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) | |
| occurrences (all) | 0 | 1 | |
| tumour pain | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 9 / 265 (3.40%) | 1 / 258 (0.39%) | |
| occurrences (all) | 13 | 1 | |
| Vascular disorders | | | |
| cyanosis | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| deep vein thrombosis | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 4 / 265 (1.51%) | 2 / 258 (0.78%) | |
| occurrences (all) | 4 | 2 | |
| embolism | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 2 / 265 (0.75%) | 0 / 258 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| flushing | | | |
| alternative dictionary used: MedDRA 26.0 | | | |

| | | |
|---|------------------|-------------------|
| subjects affected / exposed | 2 / 265 (0.75%) | 4 / 258 (1.55%) |
| occurrences (all) | 2 | 5 |
| haematoma | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) |
| occurrences (all) | 0 | 1 |
| hot flush | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 2 / 265 (0.75%) | 2 / 258 (0.78%) |
| occurrences (all) | 2 | 2 |
| hyperaemia | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) |
| occurrences (all) | 0 | 1 |
| hypotension | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 8 / 265 (3.02%) | 7 / 258 (2.71%) |
| occurrences (all) | 8 | 10 |
| hypertension | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 15 / 265 (5.66%) | 34 / 258 (13.18%) |
| occurrences (all) | 22 | 66 |
| lymphocele | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 1 / 258 (0.39%) |
| occurrences (all) | 1 | 1 |
| lymphoedema | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 2 / 265 (0.75%) | 1 / 258 (0.39%) |
| occurrences (all) | 2 | 1 |
| pallor | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) |
| occurrences (all) | 0 | 1 |

| | | | |
|---|-----------------|-----------------|--|
| pelvic venous thrombosis | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| phlebitis | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 2 / 258 (0.78%) | |
| occurrences (all) | 0 | 3 | |
| thrombosis | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) | |
| occurrences (all) | 0 | 1 | |
| venous thrombosis | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| varicose vein | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) | |
| occurrences (all) | 0 | 1 | |
| vasculitis | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 1 / 258 (0.39%) | |
| occurrences (all) | 1 | 6 | |
| vena cava thrombosis | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| venous occlusion | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Surgical and medical procedures | | | |

| | | | |
|--|----------------------|----------------------|--|
| catheter placement alternative dictionary used: MedDRA 26.0 subjects affected / exposed occurrences (all) | 0 / 265 (0.00%) 0 | 1 / 258 (0.39%) 1 | |
| central venous catheterisation alternative dictionary used: MedDRA 26.0 subjects affected / exposed occurrences (all) | 1 / 265 (0.38%) 1 | 1 / 258 (0.39%) 1 | |
| endodontic procedure alternative dictionary used: MedDRA 26.0 subjects affected / exposed occurrences (all) | 0 / 265 (0.00%) 0 | 1 / 258 (0.39%) 1 | |
| nail operation alternative dictionary used: MedDRA 26.0 subjects affected / exposed occurrences (all) | 0 / 265 (0.00%) 0 | 1 / 258 (0.39%) 1 | |
| paracentesis alternative dictionary used: MedDRA 26.0 subjects affected / exposed occurrences (all) | 0 / 265 (0.00%) 0 | 1 / 258 (0.39%) 1 | |
| skin lesion removal alternative dictionary used: MedDRA 26.0 subjects affected / exposed occurrences (all) | 0 / 265 (0.00%) 0 | 1 / 258 (0.39%) 1 | |
| tooth extraction alternative dictionary used: MedDRA 26.0 subjects affected / exposed occurrences (all) | 1 / 265 (0.38%) 1 | 0 / 258 (0.00%) 0 | |
| General disorders and administration site conditions administration site extravasation alternative dictionary used: MedDRA 26.0 subjects affected / exposed occurrences (all) administration site rash alternative dictionary used: | 0 / 265 (0.00%) 0 | 1 / 258 (0.39%) 1 | |

| | | |
|---|------------------|-------------------|
| MedDRA 26.0 | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) |
| occurrences (all) | 0 | 1 |
| asthenia | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 24 / 265 (9.06%) | 29 / 258 (11.24%) |
| occurrences (all) | 38 | 55 |
| catheter site erythema | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) |
| occurrences (all) | 0 | 1 |
| chest discomfort | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 2 / 258 (0.78%) |
| occurrences (all) | 0 | 2 |
| chest pain | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 4 / 265 (1.51%) | 1 / 258 (0.39%) |
| occurrences (all) | 4 | 1 |
| chills | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 9 / 265 (3.40%) | 6 / 258 (2.33%) |
| occurrences (all) | 12 | 7 |
| face oedema | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 3 / 258 (1.16%) |
| occurrences (all) | 1 | 3 |
| extravasation | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) |
| occurrences (all) | 2 | 0 |
| fatigue | | |
| alternative dictionary used: MedDRA 26.0 | | |

| | | |
|---|--------------------|-------------------|
| subjects affected / exposed | 106 / 265 (40.00%) | 98 / 258 (37.98%) |
| occurrences (all) | 188 | 186 |
| gait disturbance | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) |
| occurrences (all) | 1 | 0 |
| generalised oedema | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) |
| occurrences (all) | 0 | 2 |
| general physical health deterioration | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 2 / 265 (0.75%) | 1 / 258 (0.39%) |
| occurrences (all) | 2 | 1 |
| hypothermia | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) |
| occurrences (all) | 0 | 1 |
| injection site reaction | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 5 / 258 (1.94%) |
| occurrences (all) | 1 | 12 |
| injection site extravasation | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) |
| occurrences (all) | 0 | 1 |
| infusion site reaction | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) |
| occurrences (all) | 0 | 2 |
| infusion site extravasation | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 4 / 258 (1.55%) |
| occurrences (all) | 0 | 4 |

| | | |
|---|------------------|------------------|
| influenza like illness | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 7 / 265 (2.64%) | 14 / 258 (5.43%) |
| occurrences (all) | 7 | 15 |
| localised oedema | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 6 / 265 (2.26%) | 1 / 258 (0.39%) |
| occurrences (all) | 6 | 2 |
| malaise | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 10 / 265 (3.77%) | 18 / 258 (6.98%) |
| occurrences (all) | 16 | 31 |
| moaning | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) |
| occurrences (all) | 1 | 0 |
| mucosal disorder | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) |
| occurrences (all) | 0 | 2 |
| mucosal inflammation | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 4 / 265 (1.51%) | 13 / 258 (5.04%) |
| occurrences (all) | 7 | 26 |
| nodule | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) |
| occurrences (all) | 1 | 0 |
| non-cardiac chest pain | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 4 / 265 (1.51%) | 4 / 258 (1.55%) |
| occurrences (all) | 6 | 4 |
| oedema peripheral | | |
| alternative dictionary used: MedDRA 26.0 | | |

| | | |
|---|-------------------|-------------------|
| subjects affected / exposed | 34 / 265 (12.83%) | 38 / 258 (14.73%) |
| occurrences (all) | 44 | 52 |
| pain | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 8 / 265 (3.02%) | 10 / 258 (3.88%) |
| occurrences (all) | 8 | 14 |
| oedema | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 3 / 258 (1.16%) |
| occurrences (all) | 1 | 3 |
| peripheral swelling | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 2 / 258 (0.78%) |
| occurrences (all) | 0 | 3 |
| pyrexia | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 42 / 265 (15.85%) | 44 / 258 (17.05%) |
| occurrences (all) | 63 | 66 |
| swelling | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 2 / 258 (0.78%) |
| occurrences (all) | 1 | 2 |
| swelling face | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 2 / 258 (0.78%) |
| occurrences (all) | 1 | 2 |
| tenderness | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) |
| occurrences (all) | 1 | 0 |
| thirst decreased | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) |
| occurrences (all) | 1 | 0 |

| | | | |
|---|--|--|--|
| <p>Immune system disorders</p> <p>allergy to arthropod sting</p> <p>alternative dictionary used: MedDRA 26.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>0 / 265 (0.00%)</p> <p>0</p> <p>1 / 258 (0.39%)</p> <p>1</p> <p>drug hypersensitivity</p> <p>alternative dictionary used: MedDRA 26.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>1 / 265 (0.38%)</p> <p>1</p> <p>2</p> <p>hypersensitivity</p> <p>alternative dictionary used: MedDRA 26.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>4 / 265 (1.51%)</p> <p>5</p> <p>2 / 258 (0.78%)</p> <p>2</p> <p>seasonal allergy</p> <p>alternative dictionary used: MedDRA 26.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>1 / 265 (0.38%)</p> <p>1</p> <p>1 / 258 (0.39%)</p> <p>1</p> | | | |
| <p>Reproductive system and breast disorders</p> <p>breast pain</p> <p>alternative dictionary used: MedDRA 26.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>1 / 265 (0.38%)</p> <p>1</p> <p>0 / 258 (0.00%)</p> <p>0</p> <p>female genital tract fistula</p> <p>alternative dictionary used: MedDRA 26.0</p> <p>subjects affected / exposed^[2]</p> <p>occurrences (all)</p> <p>0 / 265 (0.00%)</p> <p>0</p> <p>1 / 49 (2.04%)</p> <p>1</p> <p>genital haemorrhage</p> <p>alternative dictionary used: MedDRA 26.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>1 / 265 (0.38%)</p> <p>3</p> <p>0 / 258 (0.00%)</p> <p>0</p> <p>genital ulceration</p> <p>alternative dictionary used: MedDRA 26.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>0 / 265 (0.00%)</p> <p>0</p> <p>1 / 258 (0.39%)</p> <p>1</p> <p>gynaecomastia</p> | | | |

| | | | |
|---|-----------------|-----------------|--|
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed ^[3] | 1 / 214 (0.47%) | 1 / 209 (0.48%) | |
| occurrences (all) | 1 | 1 | |
| intermenstrual bleeding | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed ^[4] | 0 / 265 (0.00%) | 1 / 49 (2.04%) | |
| occurrences (all) | 0 | 2 | |
| oedema genital | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 1 / 258 (0.39%) | |
| occurrences (all) | 1 | 1 | |
| pelvic discomfort | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 1 / 258 (0.39%) | |
| occurrences (all) | 1 | 1 | |
| pelvic organ prolapse | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) | |
| occurrences (all) | 0 | 1 | |
| pelvic pain | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 4 / 265 (1.51%) | 5 / 258 (1.94%) | |
| occurrences (all) | 4 | 5 | |
| penile pain | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed ^[5] | 1 / 214 (0.47%) | 0 / 258 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| perineal pain | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| perineal ulceration | | | |
| alternative dictionary used: MedDRA 26.0 | | | |

| | | |
|---|-----------------|-----------------|
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) |
| occurrences (all) | 0 | 1 |
| scrotal oedema | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed ^[6] | 1 / 214 (0.47%) | 3 / 209 (1.44%) |
| occurrences (all) | 1 | 3 |
| scrotal pain | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed ^[7] | 0 / 265 (0.00%) | 3 / 209 (1.44%) |
| occurrences (all) | 0 | 3 |
| scrotal swelling | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed ^[8] | 1 / 214 (0.47%) | 0 / 258 (0.00%) |
| occurrences (all) | 1 | 0 |
| testicular oedema | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed ^[9] | 1 / 214 (0.47%) | 0 / 258 (0.00%) |
| occurrences (all) | 1 | 0 |
| testicular pain | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed ^[10] | 1 / 214 (0.47%) | 1 / 209 (0.48%) |
| occurrences (all) | 1 | 1 |
| vaginal haemorrhage | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed ^[11] | 1 / 51 (1.96%) | 1 / 49 (2.04%) |
| occurrences (all) | 1 | 1 |
| vulvovaginal pruritus | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed ^[12] | 0 / 265 (0.00%) | 1 / 49 (2.04%) |
| occurrences (all) | 0 | 1 |
| vulval haemorrhage | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed ^[13] | 0 / 265 (0.00%) | 1 / 49 (2.04%) |
| occurrences (all) | 0 | 1 |

| | | | |
|---|-------------------|-------------------|--|
| Respiratory, thoracic and mediastinal disorders | | | |
| aphonia | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| bronchospasm | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) | |
| occurrences (all) | 0 | 1 | |
| chronic obstructive pulmonary disease | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| chylothorax | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) | |
| occurrences (all) | 0 | 1 | |
| cough | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 26 / 265 (9.81%) | 21 / 258 (8.14%) | |
| occurrences (all) | 29 | 30 | |
| dyspnoea | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 34 / 265 (12.83%) | 32 / 258 (12.40%) | |
| occurrences (all) | 40 | 50 | |
| dysphonia | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 3 / 265 (1.13%) | 8 / 258 (3.10%) | |
| occurrences (all) | 3 | 10 | |
| dry throat | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) | |
| occurrences (all) | 0 | 1 | |
| dyspnoea exertional | | | |

| | | |
|---|------------------|-------------------|
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 3 / 265 (1.13%) | 1 / 258 (0.39%) |
| occurrences (all) | 3 | 1 |
| epistaxis | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 14 / 265 (5.28%) | 39 / 258 (15.12%) |
| occurrences (all) | 16 | 56 |
| haemoptysis | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) |
| occurrences (all) | 0 | 1 |
| hiccups | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 8 / 265 (3.02%) | 14 / 258 (5.43%) |
| occurrences (all) | 8 | 21 |
| hypoxia | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 1 / 258 (0.39%) |
| occurrences (all) | 1 | 1 |
| laryngeal inflammation | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) |
| occurrences (all) | 1 | 0 |
| laryngeal pain | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) |
| occurrences (all) | 0 | 1 |
| lung opacity | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) |
| occurrences (all) | 0 | 1 |
| nasal dryness | | |
| alternative dictionary used: MedDRA 26.0 | | |

| | | |
|---|-----------------|------------------|
| subjects affected / exposed | 1 / 265 (0.38%) | 2 / 258 (0.78%) |
| occurrences (all) | 1 | 2 |
| oropharyngeal pain | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 5 / 265 (1.89%) | 10 / 258 (3.88%) |
| occurrences (all) | 5 | 11 |
| pleural effusion | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 2 / 265 (0.75%) | 4 / 258 (1.55%) |
| occurrences (all) | 2 | 4 |
| pneumonitis | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 2 / 265 (0.75%) | 4 / 258 (1.55%) |
| occurrences (all) | 2 | 4 |
| productive cough | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 2 / 265 (0.75%) | 4 / 258 (1.55%) |
| occurrences (all) | 2 | 5 |
| pulmonary embolism | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 2 / 265 (0.75%) | 2 / 258 (0.78%) |
| occurrences (all) | 2 | 2 |
| pulmonary fibrosis | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) |
| occurrences (all) | 0 | 1 |
| pulmonary haemorrhage | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) |
| occurrences (all) | 1 | 0 |
| rhinorrhoea | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 6 / 265 (2.26%) | 7 / 258 (2.71%) |
| occurrences (all) | 6 | 8 |

| | | | |
|---|----------------------|----------------------|--|
| respiratory tract congestion alternative dictionary used: MedDRA 26.0 subjects affected / exposed occurrences (all) | 1 / 265 (0.38%) 1 | 0 / 258 (0.00%) 0 | |
| rhinitis allergic alternative dictionary used: MedDRA 26.0 subjects affected / exposed occurrences (all) | 3 / 265 (1.13%) 3 | 3 / 258 (1.16%) 3 | |
| sinus congestion alternative dictionary used: MedDRA 26.0 subjects affected / exposed occurrences (all) | 0 / 265 (0.00%) 0 | 1 / 258 (0.39%) 1 | |
| tracheal inflammation alternative dictionary used: MedDRA 26.0 subjects affected / exposed occurrences (all) | 1 / 265 (0.38%) 1 | 0 / 258 (0.00%) 0 | |
| upper respiratory tract congestion alternative dictionary used: MedDRA 26.0 subjects affected / exposed occurrences (all) | 0 / 265 (0.00%) 0 | 1 / 258 (0.39%) 1 | |
| upper respiratory tract inflammation alternative dictionary used: MedDRA 26.0 subjects affected / exposed occurrences (all) | 1 / 265 (0.38%) 1 | 0 / 258 (0.00%) 0 | |
| upper-airway cough syndrome alternative dictionary used: MedDRA 26.0 subjects affected / exposed occurrences (all) | 2 / 265 (0.75%) 3 | 0 / 258 (0.00%) 0 | |
| wheezing alternative dictionary used: MedDRA 26.0 subjects affected / exposed occurrences (all) | 2 / 265 (0.75%) 2 | 1 / 258 (0.39%) 1 | |
| Psychiatric disorders | | | |

| | | | |
|---|-----------------|-----------------|--|
| anxiety | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 8 / 265 (3.02%) | 6 / 258 (2.33%) | |
| occurrences (all) | 10 | 6 | |
| confusional state | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 3 / 265 (1.13%) | 1 / 258 (0.39%) | |
| occurrences (all) | 4 | 1 | |
| depressive symptom | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) | |
| occurrences (all) | 0 | 1 | |
| depression | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 4 / 265 (1.51%) | 3 / 258 (1.16%) | |
| occurrences (all) | 4 | 3 | |
| delirium | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 1 / 258 (0.39%) | |
| occurrences (all) | 1 | 1 | |
| disorientation | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| emotional distress | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| euphoric mood | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| insomnia | | | |
| alternative dictionary used: MedDRA 26.0 | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 10 / 265 (3.77%) | 23 / 258 (8.91%) | |
| occurrences (all) | 11 | 25 | |
| irritability | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 2 / 258 (0.78%) | |
| occurrences (all) | 0 | 2 | |
| restlessness | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| sleep disorder | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 1 / 258 (0.39%) | |
| occurrences (all) | 1 | 1 | |
| sleep talking | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) | |
| occurrences (all) | 0 | 1 | |
| Product issues | | | |
| device occlusion | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) | |
| occurrences (all) | 0 | 1 | |
| Hepatobiliary disorders | | | |
| cholelithiasis | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) | |
| occurrences (all) | 0 | 1 | |
| hepatic failure | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) | |
| occurrences (all) | 0 | 1 | |
| hepatic function abnormal | | | |
| alternative dictionary used: MedDRA 26.0 | | | |

| | | | |
|--|-----------------------------------|-----------------------------------|--|
| <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>1 / 265 (0.38%)</p> <p>1</p> | <p>0 / 258 (0.00%)</p> <p>0</p> | |
| <p>hepatic pain</p> <p>alternative dictionary used: MedDRA 26.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>0 / 265 (0.00%)</p> <p>0</p> | <p>1 / 258 (0.39%)</p> <p>1</p> | |
| <p>jaundice</p> <p>alternative dictionary used: MedDRA 26.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>1 / 265 (0.38%)</p> <p>1</p> | <p>1 / 258 (0.39%)</p> <p>1</p> | |
| Investigations | | | |
| <p>activated partial thromboplastin time prolonged</p> <p>alternative dictionary used: MedDRA 26.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>0 / 265 (0.00%)</p> <p>0</p> | <p>1 / 258 (0.39%)</p> <p>1</p> | |
| <p>alanine aminotransferase increased</p> <p>alternative dictionary used: MedDRA 26.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>8 / 265 (3.02%)</p> <p>8</p> | <p>9 / 258 (3.49%)</p> <p>9</p> | |
| <p>aspartate aminotransferase increased</p> <p>alternative dictionary used: MedDRA 26.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>9 / 265 (3.40%)</p> <p>9</p> | <p>11 / 258 (4.26%)</p> <p>12</p> | |
| <p>blood alkaline phosphatase</p> <p>alternative dictionary used: MedDRA 26.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>1 / 265 (0.38%)</p> <p>1</p> | <p>0 / 258 (0.00%)</p> <p>0</p> | |
| <p>blood alkaline phosphatase increased</p> <p>alternative dictionary used: MedDRA 26.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>11 / 265 (4.15%)</p> <p>14</p> | <p>4 / 258 (1.55%)</p> <p>4</p> | |
| <p>blood bilirubin increased</p> <p>alternative dictionary used: MedDRA 26.0</p> | | | |

| | | |
|--|------------------|-----------------|
| subjects affected / exposed | 1 / 265 (0.38%) | 2 / 258 (0.78%) |
| occurrences (all) | 1 | 6 |
| blood calcium decreased | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) |
| occurrences (all) | 1 | 0 |
| blood creatine increased | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) |
| occurrences (all) | 1 | 0 |
| blood creatinine increased | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 21 / 265 (7.92%) | 8 / 258 (3.10%) |
| occurrences (all) | 31 | 8 |
| blood lactate dehydrogenase increased | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 2 / 258 (0.78%) |
| occurrences (all) | 0 | 2 |
| blood pressure decreased | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) |
| occurrences (all) | 1 | 0 |
| blood pressure increased | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 3 / 265 (1.13%) | 3 / 258 (1.16%) |
| occurrences (all) | 7 | 9 |
| blood thyroid stimulating hormone increased | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) |
| occurrences (all) | 1 | 0 |
| blood urea increased | | |
| alternative dictionary used: MedDRA 26.0 | | |

| | | |
|---|------------------|-----------------|
| subjects affected / exposed | 2 / 265 (0.75%) | 0 / 258 (0.00%) |
| occurrences (all) | 2 | 0 |
| blood uric acid increased | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) |
| occurrences (all) | 1 | 0 |
| body temperature increased | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) |
| occurrences (all) | 0 | 1 |
| carbon dioxide decreased | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 2 / 258 (0.78%) |
| occurrences (all) | 0 | 3 |
| clostridium test positive | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) |
| occurrences (all) | 0 | 1 |
| creatinine renal clearance decreased | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) |
| occurrences (all) | 2 | 0 |
| electrocardiogram st segment depression | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) |
| occurrences (all) | 1 | 0 |
| gamma-glutamyltransferase increased | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 10 / 265 (3.77%) | 1 / 258 (0.39%) |
| occurrences (all) | 13 | 1 |
| heart rate increased | | |
| alternative dictionary used: MedDRA 26.0 | | |

| | | |
|--|-------------------|-------------------|
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) |
| occurrences (all) | 0 | 1 |
| international normalised ratio increased | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 1 / 258 (0.39%) |
| occurrences (all) | 1 | 1 |
| lymphocyte count decreased | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 8 / 265 (3.02%) | 5 / 258 (1.94%) |
| occurrences (all) | 26 | 15 |
| lymphocyte count increased | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) |
| occurrences (all) | 2 | 0 |
| neutrophil count decreased | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 29 / 265 (10.94%) | 29 / 258 (11.24%) |
| occurrences (all) | 71 | 93 |
| neutrophil count increased | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) |
| occurrences (all) | 1 | 0 |
| platelet count decreased | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 6 / 265 (2.26%) | 21 / 258 (8.14%) |
| occurrences (all) | 9 | 56 |
| platelet count increased | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) |
| occurrences (all) | 1 | 0 |
| protein total increased | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) |
| occurrences (all) | 0 | 1 |

| | | |
|---|------------------|------------------|
| protein urine | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) |
| occurrences (all) | 0 | 1 |
| protein urine present | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) |
| occurrences (all) | 0 | 4 |
| prothrombin time prolonged | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) |
| occurrences (all) | 0 | 1 |
| total lung capacity decreased | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) |
| occurrences (all) | 1 | 0 |
| troponin t increased | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) |
| occurrences (all) | 1 | 0 |
| weight increased | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 3 / 265 (1.13%) | 1 / 258 (0.39%) |
| occurrences (all) | 3 | 1 |
| weight decreased | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 21 / 265 (7.92%) | 23 / 258 (8.91%) |
| occurrences (all) | 28 | 26 |
| white blood cells urine positive | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) |
| occurrences (all) | 0 | 1 |
| white blood cells urine | | |
| alternative dictionary used: MedDRA 26.0 | | |

| | | | |
|--|-----------------------------------|-----------------------------------|--|
| <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>0 / 265 (0.00%)</p> <p>0</p> | <p>1 / 258 (0.39%)</p> <p>1</p> | |
| <p>white blood cell count increased</p> <p>alternative dictionary used: MedDRA 26.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>1 / 265 (0.38%)</p> <p>1</p> | <p>0 / 258 (0.00%)</p> <p>0</p> | |
| <p>white blood cell count decreased</p> <p>alternative dictionary used: MedDRA 26.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>21 / 265 (7.92%)</p> <p>54</p> | <p>19 / 258 (7.36%)</p> <p>77</p> | |
| <p>Injury, poisoning and procedural complications</p> <p>contusion</p> <p>alternative dictionary used: MedDRA 26.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>1 / 265 (0.38%)</p> <p>1</p> | <p>2 / 258 (0.78%)</p> <p>2</p> | |
| <p>eschar</p> <p>alternative dictionary used: MedDRA 26.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>1 / 265 (0.38%)</p> <p>1</p> | <p>0 / 258 (0.00%)</p> <p>0</p> | |
| <p>fall</p> <p>alternative dictionary used: MedDRA 26.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>1 / 265 (0.38%)</p> <p>1</p> | <p>3 / 258 (1.16%)</p> <p>3</p> | |
| <p>fracture</p> <p>alternative dictionary used: MedDRA 26.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>0 / 265 (0.00%)</p> <p>0</p> | <p>1 / 258 (0.39%)</p> <p>1</p> | |
| <p>head injury</p> <p>alternative dictionary used: MedDRA 26.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>0 / 265 (0.00%)</p> <p>0</p> | <p>1 / 258 (0.39%)</p> <p>1</p> | |
| <p>infusion related reaction</p> <p>alternative dictionary used: MedDRA 26.0</p> | | | |

| | | |
|---|-----------------|-----------------|
| subjects affected / exposed | 6 / 265 (2.26%) | 7 / 258 (2.71%) |
| occurrences (all) | 6 | 9 |
| jaw fracture | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) |
| occurrences (all) | 1 | 0 |
| joint injury | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) |
| occurrences (all) | 0 | 1 |
| limb injury | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) |
| occurrences (all) | 0 | 1 |
| nail injury | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) |
| occurrences (all) | 0 | 1 |
| pelvic fracture | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) |
| occurrences (all) | 0 | 1 |
| penis injury | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed ^[14] | 1 / 214 (0.47%) | 0 / 258 (0.00%) |
| occurrences (all) | 1 | 0 |
| periorbital haematoma | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) |
| occurrences (all) | 0 | 1 |
| post procedural haemorrhage | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 3 / 258 (1.16%) |
| occurrences (all) | 0 | 3 |

| | | |
|---|-----------------|-----------------|
| procedural pain | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 1 / 258 (0.39%) |
| occurrences (all) | 1 | 1 |
| procedural nausea | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) |
| occurrences (all) | 1 | 0 |
| rib fracture | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) |
| occurrences (all) | 1 | 0 |
| skin abrasion | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 2 / 265 (0.75%) | 1 / 258 (0.39%) |
| occurrences (all) | 2 | 1 |
| spinal fracture | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) |
| occurrences (all) | 1 | 0 |
| thermal burn | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) |
| occurrences (all) | 1 | 0 |
| stoma site pain | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) |
| occurrences (all) | 0 | 1 |
| urinary tract stoma complication | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) |
| occurrences (all) | 0 | 1 |
| vascular access complication | | |
| alternative dictionary used: MedDRA 26.0 | | |

| | | | |
|--|---|---|--|
| <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>wound complication</p> <p>alternative dictionary used: MedDRA 26.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>wound</p> <p>alternative dictionary used: MedDRA 26.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>1 / 265 (0.38%)</p> <p>1</p> <p>0 / 265 (0.00%)</p> <p>0</p> <p>0 / 265 (0.00%)</p> <p>0</p> | <p>0 / 258 (0.00%)</p> <p>0</p> <p>1 / 258 (0.39%)</p> <p>1</p> <p>1 / 258 (0.39%)</p> <p>1</p> | |
| <p>Congenital, familial and genetic disorders</p> <p>haemophilia</p> <p>alternative dictionary used: MedDRA 26.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>0 / 265 (0.00%)</p> <p>0</p> | <p>1 / 258 (0.39%)</p> <p>1</p> | |
| <p>Cardiac disorders</p> <p>angina pectoris</p> <p>alternative dictionary used: MedDRA 26.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>atrial fibrillation</p> <p>alternative dictionary used: MedDRA 26.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>atrioventricular block first degree</p> <p>alternative dictionary used: MedDRA 26.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>arrhythmia</p> <p>alternative dictionary used: MedDRA 26.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>cardiac failure</p> <p>alternative dictionary used: MedDRA 26.0</p> | <p>0 / 265 (0.00%)</p> <p>0</p> <p>1 / 265 (0.38%)</p> <p>1</p> <p>2 / 265 (0.75%)</p> <p>2</p> <p>1 / 265 (0.38%)</p> <p>1</p> | <p>1 / 258 (0.39%)</p> <p>1</p> <p>1 / 258 (0.39%)</p> <p>1</p> <p>0 / 258 (0.00%)</p> <p>0</p> <p>0 / 258 (0.00%)</p> <p>0</p> | |

| | | |
|---|-----------------|-----------------|
| subjects affected / exposed | 0 / 265 (0.00%) | 2 / 258 (0.78%) |
| occurrences (all) | 0 | 2 |
| cardiovascular disorder | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) |
| occurrences (all) | 1 | 0 |
| bradycardia | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) |
| occurrences (all) | 0 | 1 |
| left ventricular dysfunction | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) |
| occurrences (all) | 0 | 1 |
| palpitations | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 2 / 265 (0.75%) | 2 / 258 (0.78%) |
| occurrences (all) | 2 | 3 |
| pericardial effusion | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) |
| occurrences (all) | 1 | 0 |
| sinus bradycardia | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 1 / 258 (0.39%) |
| occurrences (all) | 1 | 1 |
| sinus tachycardia | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 4 / 265 (1.51%) | 0 / 258 (0.00%) |
| occurrences (all) | 4 | 0 |
| right atrial enlargement | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) |
| occurrences (all) | 1 | 0 |

| | | | |
|--|----------------------|----------------------|--|
| tachyarrhythmia alternative dictionary used: MedDRA 26.0 subjects affected / exposed occurrences (all) | 1 / 265 (0.38%) 1 | 0 / 258 (0.00%) 0 | |
| tachycardia alternative dictionary used: MedDRA 26.0 subjects affected / exposed occurrences (all) | 2 / 265 (0.75%) 2 | 3 / 258 (1.16%) 3 | |
| Nervous system disorders ageusia alternative dictionary used: MedDRA 26.0 subjects affected / exposed occurrences (all) | 3 / 265 (1.13%) 3 | 0 / 258 (0.00%) 0 | |
| amnesia alternative dictionary used: MedDRA 26.0 subjects affected / exposed occurrences (all) | 1 / 265 (0.38%) 1 | 1 / 258 (0.39%) 1 | |
| ataxia alternative dictionary used: MedDRA 26.0 subjects affected / exposed occurrences (all) | 1 / 265 (0.38%) 1 | 0 / 258 (0.00%) 0 | |
| clonus alternative dictionary used: MedDRA 26.0 subjects affected / exposed occurrences (all) | 1 / 265 (0.38%) 2 | 0 / 258 (0.00%) 0 | |
| depressed level of consciousness alternative dictionary used: MedDRA 26.0 subjects affected / exposed occurrences (all) | 1 / 265 (0.38%) 3 | 0 / 258 (0.00%) 0 | |
| drooling alternative dictionary used: MedDRA 26.0 subjects affected / exposed occurrences (all) | 1 / 265 (0.38%) 1 | 0 / 258 (0.00%) 0 | |
| dizziness postural alternative dictionary used: MedDRA 26.0 | | | |

| | | |
|---|------------------|-------------------|
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) |
| occurrences (all) | 1 | 0 |
| dizziness | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 9 / 265 (3.40%) | 7 / 258 (2.71%) |
| occurrences (all) | 9 | 8 |
| disturbance in attention | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 2 / 258 (0.78%) |
| occurrences (all) | 0 | 2 |
| dysgeusia | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 18 / 265 (6.79%) | 28 / 258 (10.85%) |
| occurrences (all) | 19 | 41 |
| dysarthria | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) |
| occurrences (all) | 0 | 2 |
| dysaesthesia | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) |
| occurrences (all) | 0 | 1 |
| head titubation | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) |
| occurrences (all) | 2 | 0 |
| headache | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 14 / 265 (5.28%) | 19 / 258 (7.36%) |
| occurrences (all) | 15 | 27 |
| hypoesthesia | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 3 / 265 (1.13%) | 2 / 258 (0.78%) |
| occurrences (all) | 3 | 2 |

| | | |
|---|------------------|-----------------|
| hypotonia | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) |
| occurrences (all) | 1 | 0 |
| lethargy | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 3 / 258 (1.16%) |
| occurrences (all) | 1 | 3 |
| memory impairment | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 2 / 258 (0.78%) |
| occurrences (all) | 1 | 2 |
| nervous system disorder | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) |
| occurrences (all) | 1 | 0 |
| neuralgia | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) |
| occurrences (all) | 0 | 1 |
| neuropathy peripheral | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 13 / 265 (4.91%) | 7 / 258 (2.71%) |
| occurrences (all) | 16 | 9 |
| neurotoxicity | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 2 / 265 (0.75%) | 3 / 258 (1.16%) |
| occurrences (all) | 2 | 3 |
| paraesthesia | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 14 / 265 (5.28%) | 5 / 258 (1.94%) |
| occurrences (all) | 15 | 7 |
| peripheral sensory neuropathy | | |
| alternative dictionary used: MedDRA 26.0 | | |

| | | |
|---|------------------|------------------|
| subjects affected / exposed | 22 / 265 (8.30%) | 18 / 258 (6.98%) |
| occurrences (all) | 31 | 23 |
| peroneal nerve palsy | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) |
| occurrences (all) | 0 | 1 |
| polyneuropathy | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) |
| occurrences (all) | 0 | 1 |
| peripheral motor neuropathy | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 2 / 265 (0.75%) | 1 / 258 (0.39%) |
| occurrences (all) | 2 | 1 |
| presyncope | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) |
| occurrences (all) | 0 | 1 |
| radiculopathy | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) |
| occurrences (all) | 1 | 0 |
| sciatica | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 1 / 258 (0.39%) |
| occurrences (all) | 1 | 1 |
| syncope | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 2 / 265 (0.75%) | 0 / 258 (0.00%) |
| occurrences (all) | 2 | 0 |
| taste disorder | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 2 / 258 (0.78%) |
| occurrences (all) | 1 | 2 |

| | | | |
|---|---|---|--|
| <p>somnolence</p> <p>alternative dictionary used: MedDRA 26.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>1 / 265 (0.38%)</p> <p>1</p> | <p>2 / 258 (0.78%)</p> <p>2</p> | |
| <p>tremor</p> <p>alternative dictionary used: MedDRA 26.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>3 / 265 (1.13%)</p> <p>4</p> | <p>2 / 258 (0.78%)</p> <p>3</p> | |
| <p>Blood and lymphatic system disorders</p> <p>anaemia</p> <p>alternative dictionary used: MedDRA 26.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>blood loss anaemia</p> <p>alternative dictionary used: MedDRA 26.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>febrile neutropenia</p> <p>alternative dictionary used: MedDRA 26.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>leukocytosis</p> <p>alternative dictionary used: MedDRA 26.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>leukopenia</p> <p>alternative dictionary used: MedDRA 26.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>lymph node pain</p> <p>alternative dictionary used: MedDRA 26.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>lymphopenia</p> <p>alternative dictionary used: MedDRA 26.0</p> | <p>76 / 265 (28.68%)</p> <p>140</p> <p>0 / 265 (0.00%)</p> <p>0</p> <p>5 / 265 (1.89%)</p> <p>5</p> <p>3 / 265 (1.13%)</p> <p>3</p> <p>5 / 265 (1.89%)</p> <p>9</p> <p>1 / 265 (0.38%)</p> <p>1</p> | <p>50 / 258 (19.38%)</p> <p>87</p> <p>1 / 258 (0.39%)</p> <p>1</p> <p>9 / 258 (3.49%)</p> <p>9</p> <p>1 / 258 (0.39%)</p> <p>1</p> <p>8 / 258 (3.10%)</p> <p>25</p> <p>0 / 258 (0.00%)</p> <p>0</p> | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 2 / 265 (0.75%) | 2 / 258 (0.78%) | |
| occurrences (all) | 2 | 7 | |
| neutropenia | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 14 / 265 (5.28%) | 18 / 258 (6.98%) | |
| occurrences (all) | 14 | 36 | |
| thrombocytopenia | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 3 / 265 (1.13%) | 6 / 258 (2.33%) | |
| occurrences (all) | 3 | 13 | |
| thrombocytosis | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Ear and labyrinth disorders | | | |
| ear discomfort | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 2 / 265 (0.75%) | 0 / 258 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| ear canal stenosis | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| hypoacusis | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| middle ear inflammation | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) | |
| occurrences (all) | 0 | 1 | |
| otorrhoea | | | |
| alternative dictionary used: MedDRA 26.0 | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| tinnitus | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 1 / 258 (0.39%) | |
| occurrences (all) | 1 | 1 | |
| vestibular disorder | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| vertigo | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 3 / 265 (1.13%) | 0 / 258 (0.00%) | |
| occurrences (all) | 4 | 0 | |
| Eye disorders | | | |
| dry eye | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 2 / 265 (0.75%) | 3 / 258 (1.16%) | |
| occurrences (all) | 2 | 3 | |
| eczema eyelids | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) | |
| occurrences (all) | 0 | 1 | |
| eye discharge | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) | |
| occurrences (all) | 0 | 1 | |
| eye disorder | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| eye pain | | | |
| alternative dictionary used: MedDRA 26.0 | | | |

| | | |
|---|------------------|------------------|
| subjects affected / exposed | 0 / 265 (0.00%) | 2 / 258 (0.78%) |
| occurrences (all) | 0 | 4 |
| eye pruritus | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 1 / 258 (0.39%) |
| occurrences (all) | 1 | 1 |
| eyelid function disorder | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) |
| occurrences (all) | 0 | 1 |
| eyelid oedema | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) |
| occurrences (all) | 1 | 0 |
| eyelid ptosis | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) |
| occurrences (all) | 1 | 0 |
| glaucoma | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) |
| occurrences (all) | 1 | 0 |
| lacrimation increased | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 12 / 265 (4.53%) | 24 / 258 (9.30%) |
| occurrences (all) | 12 | 28 |
| ocular discomfort | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) |
| occurrences (all) | 1 | 0 |
| photopsia | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) |
| occurrences (all) | 0 | 1 |

| | | | |
|---|----------------------|----------------------|--|
| retinal vascular disorder alternative dictionary used: MedDRA 26.0 subjects affected / exposed occurrences (all) | 1 / 265 (0.38%) 2 | 0 / 258 (0.00%) 0 | |
| vitreous haemorrhage alternative dictionary used: MedDRA 26.0 subjects affected / exposed occurrences (all) | 0 / 265 (0.00%) 0 | 1 / 258 (0.39%) 1 | |
| vitreous detachment alternative dictionary used: MedDRA 26.0 subjects affected / exposed occurrences (all) | 1 / 265 (0.38%) 1 | 0 / 258 (0.00%) 0 | |
| visual impairment alternative dictionary used: MedDRA 26.0 subjects affected / exposed occurrences (all) | 1 / 265 (0.38%) 1 | 0 / 258 (0.00%) 0 | |
| vision blurred alternative dictionary used: MedDRA 26.0 subjects affected / exposed occurrences (all) | 1 / 265 (0.38%) 1 | 3 / 258 (1.16%) 3 | |
| Gastrointestinal disorders abdominal discomfort alternative dictionary used: MedDRA 26.0 subjects affected / exposed occurrences (all) | 0 / 265 (0.00%) 0 | 2 / 258 (0.78%) 2 | |
| abdominal distension alternative dictionary used: MedDRA 26.0 subjects affected / exposed occurrences (all) | 5 / 265 (1.89%) 5 | 7 / 258 (2.71%) 7 | |
| abdominal wall disorder alternative dictionary used: MedDRA 26.0 subjects affected / exposed occurrences (all) | 1 / 265 (0.38%) 2 | 0 / 258 (0.00%) 0 | |
| abdominal pain lower alternative dictionary used: MedDRA 26.0 | | | |

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|---|------------------|------------------|
| subjects affected / exposed | 1 / 265 (0.38%) | 1 / 258 (0.39%) |
| occurrences (all) | 1 | 1 |
| abdominal pain upper | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 10 / 265 (3.77%) | 12 / 258 (4.65%) |
| occurrences (all) | 10 | 15 |
| abdominal pain | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 17 / 265 (6.42%) | 20 / 258 (7.75%) |
| occurrences (all) | 22 | 26 |
| anal fistula | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) |
| occurrences (all) | 0 | 1 |
| anal haemorrhage | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) |
| occurrences (all) | 0 | 1 |
| anal incontinence | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) |
| occurrences (all) | 1 | 0 |
| anal inflammation | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 1 / 258 (0.39%) |
| occurrences (all) | 1 | 1 |
| angular cheilitis | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) |
| occurrences (all) | 1 | 0 |
| ascites | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 7 / 258 (2.71%) |
| occurrences (all) | 1 | 8 |

| | | |
|---|-------------------|-------------------|
| cheilitis | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) |
| occurrences (all) | 0 | 1 |
| colitis | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) |
| occurrences (all) | 0 | 1 |
| constipation | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 45 / 265 (16.98%) | 35 / 258 (13.57%) |
| occurrences (all) | 58 | 46 |
| diarrhoea | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 56 / 265 (21.13%) | 81 / 258 (31.40%) |
| occurrences (all) | 81 | 131 |
| dysphagia | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 2 / 265 (0.75%) | 6 / 258 (2.33%) |
| occurrences (all) | 2 | 6 |
| dyspepsia | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 7 / 265 (2.64%) | 9 / 258 (3.49%) |
| occurrences (all) | 7 | 10 |
| dyschezia | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) |
| occurrences (all) | 0 | 1 |
| dry mouth | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 5 / 265 (1.89%) | 11 / 258 (4.26%) |
| occurrences (all) | 5 | 13 |
| ectopic gastric mucosa | | |
| alternative dictionary used: MedDRA 26.0 | | |

| | | |
|---|-----------------|-----------------|
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) |
| occurrences (all) | 1 | 0 |
| eructation | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) |
| occurrences (all) | 1 | 0 |
| epigastric discomfort | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) |
| occurrences (all) | 1 | 0 |
| enterocolitis | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) |
| occurrences (all) | 0 | 1 |
| flatulence | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 1 / 258 (0.39%) |
| occurrences (all) | 1 | 1 |
| faeces discoloured | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) |
| occurrences (all) | 0 | 1 |
| gastrointestinal obstruction | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) |
| occurrences (all) | 0 | 1 |
| gastrointestinal motility disorder | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) |
| occurrences (all) | 0 | 1 |
| gastritis | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) |
| occurrences (all) | 0 | 1 |

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|---|-----------------|-----------------|
| gastric polyps | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) |
| occurrences (all) | 1 | 0 |
| food poisoning | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) |
| occurrences (all) | 0 | 1 |
| gastrooesophageal reflux disease | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 4 / 265 (1.51%) | 3 / 258 (1.16%) |
| occurrences (all) | 4 | 8 |
| gingival atrophy | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) |
| occurrences (all) | 0 | 1 |
| gingival bleeding | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 3 / 258 (1.16%) |
| occurrences (all) | 0 | 3 |
| haematochezia | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 2 / 265 (0.75%) | 3 / 258 (1.16%) |
| occurrences (all) | 2 | 3 |
| glossitis | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) |
| occurrences (all) | 0 | 1 |
| gingival pain | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) |
| occurrences (all) | 0 | 2 |
| hiatus hernia | | |
| alternative dictionary used: MedDRA 26.0 | | |

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|---|-----------------|-----------------|
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) |
| occurrences (all) | 1 | 0 |
| hyperchlorhydria | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) |
| occurrences (all) | 1 | 0 |
| haemorrhoidal haemorrhage | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) |
| occurrences (all) | 0 | 1 |
| haemorrhoids | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 2 / 265 (0.75%) | 8 / 258 (3.10%) |
| occurrences (all) | 2 | 9 |
| ileus | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 2 / 258 (0.78%) |
| occurrences (all) | 1 | 2 |
| intestinal haemorrhage | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) |
| occurrences (all) | 0 | 1 |
| intra-abdominal haematoma | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) |
| occurrences (all) | 1 | 0 |
| large intestinal haemorrhage | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) |
| occurrences (all) | 1 | 0 |
| lip blister | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) |
| occurrences (all) | 0 | 1 |

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|---|-------------------|-------------------|
| mouth ulceration | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 1 / 258 (0.39%) |
| occurrences (all) | 1 | 1 |
| melaena | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 1 / 258 (0.39%) |
| occurrences (all) | 2 | 1 |
| lip dry | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) |
| occurrences (all) | 0 | 1 |
| mucous stools | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) |
| occurrences (all) | 0 | 1 |
| odynophagia | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 2 / 265 (0.75%) | 0 / 258 (0.00%) |
| occurrences (all) | 2 | 0 |
| nausea | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 55 / 265 (20.75%) | 71 / 258 (27.52%) |
| occurrences (all) | 82 | 102 |
| obstruction gastric | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) |
| occurrences (all) | 0 | 5 |
| oral disorder | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) |
| occurrences (all) | 0 | 1 |
| oral hyperaesthesia | | |
| alternative dictionary used: MedDRA 26.0 | | |

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|---|-------------------|-------------------|
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) |
| occurrences (all) | 0 | 1 |
| oral pain | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 2 / 265 (0.75%) | 1 / 258 (0.39%) |
| occurrences (all) | 2 | 1 |
| periodontal disease | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 2 / 265 (0.75%) | 1 / 258 (0.39%) |
| occurrences (all) | 2 | 2 |
| proctalgia | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 2 / 258 (0.78%) |
| occurrences (all) | 1 | 2 |
| proctitis | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) |
| occurrences (all) | 0 | 1 |
| rectal haemorrhage | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 3 / 265 (1.13%) | 1 / 258 (0.39%) |
| occurrences (all) | 3 | 1 |
| rectal prolapse | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) |
| occurrences (all) | 0 | 1 |
| rectal tenesmus | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 2 / 258 (0.78%) |
| occurrences (all) | 1 | 2 |
| stomatitis | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 30 / 265 (11.32%) | 66 / 258 (25.58%) |
| occurrences (all) | 36 | 117 |

| | | | |
|---|--------------------------|-------------------------|--|
| toothache alternative dictionary used: MedDRA 26.0 subjects affected / exposed occurrences (all) | 4 / 265 (1.51%) 4 | 1 / 258 (0.39%) 1 | |
| upper gastrointestinal haemorrhage alternative dictionary used: MedDRA 26.0 subjects affected / exposed occurrences (all) | 0 / 265 (0.00%) 0 | 1 / 258 (0.39%) 1 | |
| vomiting alternative dictionary used: MedDRA 26.0 subjects affected / exposed occurrences (all) | 40 / 265 (15.09%) 56 | 41 / 258 (15.89%) 62 | |
| Skin and subcutaneous tissue disorders acne alternative dictionary used: MedDRA 26.0 subjects affected / exposed occurrences (all) | 0 / 265 (0.00%) 0 | 1 / 258 (0.39%) 1 | |
| alopecia alternative dictionary used: MedDRA 26.0 subjects affected / exposed occurrences (all) | 94 / 265 (35.47%) 115 | 66 / 258 (25.58%) 79 | |
| dermatitis alternative dictionary used: MedDRA 26.0 subjects affected / exposed occurrences (all) | 0 / 265 (0.00%) 0 | 1 / 258 (0.39%) 1 | |
| decubitus ulcer alternative dictionary used: MedDRA 26.0 subjects affected / exposed occurrences (all) | 0 / 265 (0.00%) 0 | 1 / 258 (0.39%) 1 | |
| dermatitis acneiform alternative dictionary used: MedDRA 26.0 subjects affected / exposed occurrences (all) | 1 / 265 (0.38%) 1 | 0 / 258 (0.00%) 0 | |
| dry skin alternative dictionary used: MedDRA 26.0 | | | |

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|---|-----------------|------------------|
| subjects affected / exposed | 6 / 265 (2.26%) | 11 / 258 (4.26%) |
| occurrences (all) | 6 | 12 |
| drug eruption | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) |
| occurrences (all) | 0 | 1 |
| eczema | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 2 / 258 (0.78%) |
| occurrences (all) | 0 | 4 |
| epidermolysis | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) |
| occurrences (all) | 0 | 1 |
| erythema | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 3 / 265 (1.13%) | 6 / 258 (2.33%) |
| occurrences (all) | 3 | 7 |
| erythema multiforme | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 3 / 265 (1.13%) | 0 / 258 (0.00%) |
| occurrences (all) | 3 | 0 |
| hyperhidrosis | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 2 / 265 (0.75%) | 2 / 258 (0.78%) |
| occurrences (all) | 2 | 2 |
| nail bed disorder | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) |
| occurrences (all) | 0 | 1 |
| nail bed inflammation | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) |
| occurrences (all) | 0 | 1 |

| | | |
|---|------------------|-----------------|
| nail discolouration | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 15 / 265 (5.66%) | 7 / 258 (2.71%) |
| occurrences (all) | 15 | 7 |
| nail disorder | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 3 / 265 (1.13%) | 3 / 258 (1.16%) |
| occurrences (all) | 3 | 3 |
| nail dystrophy | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) |
| occurrences (all) | 0 | 1 |
| nail toxicity | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 2 / 258 (0.78%) |
| occurrences (all) | 1 | 4 |
| night sweats | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 2 / 265 (0.75%) | 2 / 258 (0.78%) |
| occurrences (all) | 2 | 2 |
| nail ridging | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 3 / 265 (1.13%) | 6 / 258 (2.33%) |
| occurrences (all) | 3 | 7 |
| onychalgia | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) |
| occurrences (all) | 0 | 5 |
| onycholysis | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 2 / 265 (0.75%) | 5 / 258 (1.94%) |
| occurrences (all) | 3 | 7 |
| onychomadesis | | |
| alternative dictionary used: MedDRA 26.0 | | |

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|--|------------------|------------------|
| subjects affected / exposed | 5 / 265 (1.89%) | 8 / 258 (3.10%) |
| occurrences (all) | 5 | 10 |
| onychoclasia | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) |
| occurrences (all) | 0 | 1 |
| pain of skin | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 3 / 258 (1.16%) |
| occurrences (all) | 0 | 3 |
| palmar-plantar erythrodysaesthesia syndrome | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 6 / 265 (2.26%) | 19 / 258 (7.36%) |
| occurrences (all) | 15 | 28 |
| photosensitivity reaction | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) |
| occurrences (all) | 0 | 2 |
| pruritus | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 12 / 265 (4.53%) | 10 / 258 (3.88%) |
| occurrences (all) | 17 | 11 |
| rash | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 15 / 265 (5.66%) | 11 / 258 (4.26%) |
| occurrences (all) | 18 | 14 |
| rash erythematous | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) |
| occurrences (all) | 1 | 0 |
| rash maculo-papular | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 5 / 265 (1.89%) | 0 / 258 (0.00%) |
| occurrences (all) | 5 | 0 |

| | | |
|---|-----------------|-----------------|
| skin burning sensation | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) |
| occurrences (all) | 1 | 0 |
| skin discolouration | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) |
| occurrences (all) | 1 | 0 |
| skin disorder | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) |
| occurrences (all) | 0 | 2 |
| skin exfoliation | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) |
| occurrences (all) | 0 | 1 |
| skin fissures | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) |
| occurrences (all) | 1 | 0 |
| skin hyperpigmentation | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 2 / 265 (0.75%) | 2 / 258 (0.78%) |
| occurrences (all) | 2 | 2 |
| skin lesion | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) |
| occurrences (all) | 1 | 0 |
| skin ulcer | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 2 / 258 (0.78%) |
| occurrences (all) | 0 | 3 |
| urticaria | | |
| alternative dictionary used: MedDRA 26.0 | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 4 / 265 (1.51%) | 5 / 258 (1.94%) | |
| occurrences (all) | 4 | 5 | |
| xeroderma | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) | |
| occurrences (all) | 0 | 1 | |
| Renal and urinary disorders | | | |
| acute kidney injury | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 5 / 258 (1.94%) | |
| occurrences (all) | 0 | 5 | |
| anuria | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| bladder pain | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 1 / 258 (0.39%) | |
| occurrences (all) | 1 | 1 | |
| chromaturia | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 1 / 258 (0.39%) | |
| occurrences (all) | 1 | 1 | |
| chronic kidney disease | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| cystitis noninfective | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| cystitis interstitial | | | |
| alternative dictionary used: MedDRA 26.0 | | | |

| | | |
|---|------------------|-------------------|
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) |
| occurrences (all) | 0 | 1 |
| dysuria | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 4 / 265 (1.51%) | 3 / 258 (1.16%) |
| occurrences (all) | 4 | 3 |
| haematuria | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 19 / 265 (7.17%) | 30 / 258 (11.63%) |
| occurrences (all) | 20 | 48 |
| hydronephrosis | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) |
| occurrences (all) | 0 | 1 |
| hydroureter | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) |
| occurrences (all) | 0 | 1 |
| micturition urgency | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 2 / 258 (0.78%) |
| occurrences (all) | 0 | 2 |
| nocturia | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) |
| occurrences (all) | 0 | 1 |
| pollakiuria | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 4 / 265 (1.51%) | 3 / 258 (1.16%) |
| occurrences (all) | 4 | 3 |
| polyuria | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) |
| occurrences (all) | 0 | 1 |

| | | |
|---|------------------|-------------------|
| proteinuria | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 16 / 265 (6.04%) | 33 / 258 (12.79%) |
| occurrences (all) | 28 | 60 |
| renal failure | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 2 / 265 (0.75%) | 1 / 258 (0.39%) |
| occurrences (all) | 2 | 1 |
| renal impairment | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 2 / 258 (0.78%) |
| occurrences (all) | 1 | 2 |
| renal pain | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 1 / 258 (0.39%) |
| occurrences (all) | 1 | 1 |
| urinary hesitation | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) |
| occurrences (all) | 1 | 0 |
| urethral haemorrhage | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) |
| occurrences (all) | 1 | 0 |
| urinary fistula | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) |
| occurrences (all) | 0 | 1 |
| urinary tract pain | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 2 / 265 (0.75%) | 0 / 258 (0.00%) |
| occurrences (all) | 2 | 0 |
| urinary tract obstruction | | |
| alternative dictionary used: MedDRA 26.0 | | |

| | | | |
|--|---|---|--|
| <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>urinary retention</p> <p>alternative dictionary used: MedDRA 26.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>urinary incontinence</p> <p>alternative dictionary used: MedDRA 26.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>urine odour abnormal</p> <p>alternative dictionary used: MedDRA 26.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>1 / 265 (0.38%)</p> <p>1</p> <p>5 / 265 (1.89%)</p> <p>6</p> <p>6 / 265 (2.26%)</p> <p>6</p> <p>2 / 265 (0.75%)</p> <p>2</p> | <p>2 / 258 (0.78%)</p> <p>2</p> <p>1 / 258 (0.39%)</p> <p>1</p> <p>1 / 258 (0.39%)</p> <p>1</p> <p>1 / 258 (0.39%)</p> <p>1</p> | |
| <p>Endocrine disorders</p> <p>adrenal insufficiency</p> <p>alternative dictionary used: MedDRA 26.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>hypothyroidism</p> <p>alternative dictionary used: MedDRA 26.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>1 / 265 (0.38%)</p> <p>1</p> <p>1 / 265 (0.38%)</p> <p>1</p> | <p>0 / 258 (0.00%)</p> <p>0</p> <p>2 / 258 (0.78%)</p> <p>3</p> | |
| <p>Musculoskeletal and connective tissue disorders</p> <p>arthralgia</p> <p>alternative dictionary used: MedDRA 26.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>arthritis</p> <p>alternative dictionary used: MedDRA 26.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>back pain</p> <p>alternative dictionary used: MedDRA 26.0</p> | <p>26 / 265 (9.81%)</p> <p>34</p> <p>0 / 265 (0.00%)</p> <p>0</p> | <p>30 / 258 (11.63%)</p> <p>39</p> <p>1 / 258 (0.39%)</p> <p>1</p> | |

| | | |
|---|------------------|-------------------|
| subjects affected / exposed | 21 / 265 (7.92%) | 29 / 258 (11.24%) |
| occurrences (all) | 26 | 36 |
| bone pain | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 17 / 265 (6.42%) | 15 / 258 (5.81%) |
| occurrences (all) | 19 | 15 |
| flank pain | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 5 / 265 (1.89%) | 3 / 258 (1.16%) |
| occurrences (all) | 6 | 3 |
| groin pain | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 7 / 265 (2.64%) | 4 / 258 (1.55%) |
| occurrences (all) | 7 | 6 |
| intervertebral disc disorder | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) |
| occurrences (all) | 1 | 0 |
| intervertebral disc protrusion | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) |
| occurrences (all) | 0 | 1 |
| inguinal mass | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) |
| occurrences (all) | 1 | 0 |
| joint effusion | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) |
| occurrences (all) | 0 | 1 |
| joint swelling | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) |
| occurrences (all) | 0 | 1 |

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|---|------------------|------------------|--|
| limb discomfort | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) | |
| occurrences (all) | 0 | 1 | |
| muscle fatigue | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) | |
| occurrences (all) | 0 | 1 | |
| muscle spasms | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 4 / 265 (1.51%) | 2 / 258 (0.78%) | |
| occurrences (all) | 4 | 4 | |
| muscle twitching | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| muscular weakness | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 6 / 265 (2.26%) | 5 / 258 (1.94%) | |
| occurrences (all) | 7 | 6 | |
| musculoskeletal chest pain | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 3 / 265 (1.13%) | 4 / 258 (1.55%) | |
| occurrences (all) | 3 | 4 | |
| musculoskeletal pain | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 4 / 265 (1.51%) | 1 / 258 (0.39%) | |
| occurrences (all) | 4 | 1 | |
| myalgia | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 23 / 265 (8.68%) | 24 / 258 (9.30%) | |
| occurrences (all) | 30 | 39 | |
| myofascitis | | | |
| alternative dictionary used: MedDRA 26.0 | | | |

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|---|------------------|------------------|
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) |
| occurrences (all) | 1 | 0 |
| neck mass | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) |
| occurrences (all) | 1 | 0 |
| neck pain | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 5 / 265 (1.89%) | 3 / 258 (1.16%) |
| occurrences (all) | 7 | 3 |
| osteoarthritis | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) |
| occurrences (all) | 0 | 1 |
| osteonecrosis of jaw | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) |
| occurrences (all) | 0 | 1 |
| pain in extremity | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 16 / 265 (6.04%) | 12 / 258 (4.65%) |
| occurrences (all) | 22 | 15 |
| pain in jaw | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) |
| occurrences (all) | 0 | 1 |
| polymyalgia rheumatica | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) |
| occurrences (all) | 0 | 1 |
| pubic pain | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) |
| occurrences (all) | 0 | 1 |

| | | | |
|--|----------------------|----------------------|--|
| sacral pain alternative dictionary used: MedDRA 26.0 subjects affected / exposed occurrences (all) | 1 / 265 (0.38%) 1 | 1 / 258 (0.39%) 1 | |
| spinal pain alternative dictionary used: MedDRA 26.0 subjects affected / exposed occurrences (all) | 1 / 265 (0.38%) 1 | 0 / 258 (0.00%) 0 | |
| Infections and infestations abscess intestinal alternative dictionary used: MedDRA 26.0 subjects affected / exposed occurrences (all) | 0 / 265 (0.00%) 0 | 1 / 258 (0.39%) 1 | |
| anal abscess alternative dictionary used: MedDRA 26.0 subjects affected / exposed occurrences (all) | 1 / 265 (0.38%) 1 | 0 / 258 (0.00%) 0 | |
| bacteraemia alternative dictionary used: MedDRA 26.0 subjects affected / exposed occurrences (all) | 0 / 265 (0.00%) 0 | 1 / 258 (0.39%) 1 | |
| bacteriuria alternative dictionary used: MedDRA 26.0 subjects affected / exposed occurrences (all) | 1 / 265 (0.38%) 1 | 0 / 258 (0.00%) 0 | |
| covid-19 alternative dictionary used: MedDRA 26.0 subjects affected / exposed occurrences (all) | 0 / 265 (0.00%) 0 | 1 / 258 (0.39%) 1 | |
| cellulitis alternative dictionary used: MedDRA 26.0 subjects affected / exposed occurrences (all) | 2 / 265 (0.75%) 2 | 2 / 258 (0.78%) 3 | |
| breast cellulitis alternative dictionary used: MedDRA 26.0 | | | |

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|---|-----------------|-----------------|
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) |
| occurrences (all) | 1 | 0 |
| bronchitis | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 3 / 265 (1.13%) | 4 / 258 (1.55%) |
| occurrences (all) | 3 | 4 |
| conjunctivitis | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 5 / 258 (1.94%) |
| occurrences (all) | 1 | 6 |
| cystitis | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 2 / 258 (0.78%) |
| occurrences (all) | 1 | 2 |
| device related infection | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 2 / 258 (0.78%) |
| occurrences (all) | 0 | 2 |
| dacryocystitis | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) |
| occurrences (all) | 0 | 2 |
| enterovirus infection | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) |
| occurrences (all) | 1 | 0 |
| eye infection | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 2 / 265 (0.75%) | 0 / 258 (0.00%) |
| occurrences (all) | 2 | 0 |
| gastroenteritis | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) |
| occurrences (all) | 1 | 0 |

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|---|-----------------|-----------------|
| furuncle | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 2 / 258 (0.78%) |
| occurrences (all) | 0 | 2 |
| fungus infection | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) |
| occurrences (all) | 1 | 0 |
| gingivitis | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 2 / 265 (0.75%) | 4 / 258 (1.55%) |
| occurrences (all) | 2 | 4 |
| helicobacter infection | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) |
| occurrences (all) | 0 | 1 |
| herpes dermatitis | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) |
| occurrences (all) | 0 | 1 |
| herpes virus infection | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) |
| occurrences (all) | 2 | 0 |
| herpes zoster | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 2 / 258 (0.78%) |
| occurrences (all) | 1 | 2 |
| influenza | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 3 / 258 (1.16%) |
| occurrences (all) | 1 | 3 |
| infective glossitis | | |
| alternative dictionary used: MedDRA 26.0 | | |

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|---|-----------------|-----------------|
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) |
| occurrences (all) | 0 | 1 |
| infection | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) |
| occurrences (all) | 0 | 1 |
| kidney infection | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) |
| occurrences (all) | 1 | 0 |
| lower respiratory tract infection | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) |
| occurrences (all) | 0 | 1 |
| nail bed infection | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) |
| occurrences (all) | 0 | 3 |
| nail infection | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 5 / 258 (1.94%) |
| occurrences (all) | 1 | 7 |
| mucosal infection | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 1 / 258 (0.39%) |
| occurrences (all) | 1 | 1 |
| nasopharyngitis | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 3 / 265 (1.13%) | 5 / 258 (1.94%) |
| occurrences (all) | 3 | 5 |
| onychomycosis | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) |
| occurrences (all) | 2 | 0 |

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|---|-----------------|-----------------|
| oral candidiasis | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 3 / 265 (1.13%) | 5 / 258 (1.94%) |
| occurrences (all) | 3 | 5 |
| oral fungal infection | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) |
| occurrences (all) | 0 | 1 |
| oral herpes | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) |
| occurrences (all) | 0 | 1 |
| paronychia | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 2 / 258 (0.78%) |
| occurrences (all) | 0 | 3 |
| parotitis | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) |
| occurrences (all) | 0 | 1 |
| perineal abscess | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) |
| occurrences (all) | 2 | 0 |
| perineal infection | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) |
| occurrences (all) | 0 | 2 |
| postoperative wound infection | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) |
| occurrences (all) | 0 | 1 |
| peritonitis bacterial | | |
| alternative dictionary used: MedDRA 26.0 | | |

| | | |
|---|-----------------|-----------------|
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) |
| occurrences (all) | 0 | 1 |
| pharyngitis | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 1 / 258 (0.39%) |
| occurrences (all) | 1 | 2 |
| pneumonia | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 3 / 265 (1.13%) | 1 / 258 (0.39%) |
| occurrences (all) | 5 | 1 |
| post procedural infection | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) |
| occurrences (all) | 0 | 1 |
| pyelonephritis | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) |
| occurrences (all) | 0 | 2 |
| pyelonephritis acute | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) |
| occurrences (all) | 0 | 1 |
| respiratory tract infection | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) |
| occurrences (all) | 0 | 1 |
| respiratory tract infection viral | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) |
| occurrences (all) | 0 | 1 |
| rhinitis | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 3 / 258 (1.16%) |
| occurrences (all) | 1 | 5 |

| | | |
|---|-----------------|-----------------|
| sepsis | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) |
| occurrences (all) | 1 | 0 |
| sinusitis | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 2 / 265 (0.75%) | 1 / 258 (0.39%) |
| occurrences (all) | 2 | 1 |
| skin infection | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 1 / 258 (0.39%) |
| occurrences (all) | 1 | 1 |
| spinal cord infection | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) |
| occurrences (all) | 1 | 0 |
| tooth infection | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 3 / 258 (1.16%) |
| occurrences (all) | 0 | 3 |
| tooth abscess | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 2 / 258 (0.78%) |
| occurrences (all) | 0 | 2 |
| tonsillitis | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) |
| occurrences (all) | 0 | 1 |
| tinea pedis | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) |
| occurrences (all) | 1 | 0 |
| tracheitis | | |
| alternative dictionary used: MedDRA 26.0 | | |

| | | | |
|---|-------------------|-------------------|--|
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| upper respiratory tract infection | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 9 / 265 (3.40%) | 5 / 258 (1.94%) | |
| occurrences (all) | 9 | 5 | |
| urethritis | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) | |
| occurrences (all) | 0 | 1 | |
| urinary tract infection | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 34 / 265 (12.83%) | 31 / 258 (12.02%) | |
| occurrences (all) | 39 | 38 | |
| viral upper respiratory tract infection | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| viral infection | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) | |
| occurrences (all) | 0 | 1 | |
| Metabolism and nutrition disorders | | | |
| acidosis | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| cachexia | | | |
| alternative dictionary used: MedDRA 26.0 | | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) | |
| occurrences (all) | 0 | 1 | |
| dehydration | | | |
| alternative dictionary used: MedDRA 26.0 | | | |

| | | |
|---|-------------------|-------------------|
| subjects affected / exposed | 5 / 265 (1.89%) | 8 / 258 (3.10%) |
| occurrences (all) | 5 | 8 |
| decreased appetite | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 64 / 265 (24.15%) | 82 / 258 (31.78%) |
| occurrences (all) | 82 | 128 |
| fluid retention | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 0 / 265 (0.00%) | 1 / 258 (0.39%) |
| occurrences (all) | 0 | 1 |
| gout | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 1 / 258 (0.39%) |
| occurrences (all) | 1 | 1 |
| hypercalcaemia | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 12 / 265 (4.53%) | 6 / 258 (2.33%) |
| occurrences (all) | 15 | 11 |
| hyperglycaemia | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 13 / 265 (4.91%) | 8 / 258 (3.10%) |
| occurrences (all) | 15 | 12 |
| hyperkalaemia | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 7 / 265 (2.64%) | 12 / 258 (4.65%) |
| occurrences (all) | 12 | 26 |
| hypophosphataemia | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 7 / 265 (2.64%) | 6 / 258 (2.33%) |
| occurrences (all) | 8 | 10 |
| hypophagia | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) |
| occurrences (all) | 1 | 0 |

| | | |
|---|------------------|------------------|
| hyponatraemia | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 10 / 265 (3.77%) | 7 / 258 (2.71%) |
| occurrences (all) | 11 | 10 |
| hypomagnesaemia | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 5 / 265 (1.89%) | 4 / 258 (1.55%) |
| occurrences (all) | 7 | 4 |
| hypokalaemia | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 5 / 265 (1.89%) | 3 / 258 (1.16%) |
| occurrences (all) | 7 | 3 |
| hypocalcaemia | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 4 / 265 (1.51%) | 2 / 258 (0.78%) |
| occurrences (all) | 6 | 2 |
| hypoalbuminaemia | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 26 / 265 (9.81%) | 17 / 258 (6.59%) |
| occurrences (all) | 32 | 25 |
| hyperuricaemia | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 15 / 265 (5.66%) | 10 / 258 (3.88%) |
| occurrences (all) | 17 | 11 |
| hypernatraemia | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 0 / 258 (0.00%) |
| occurrences (all) | 1 | 0 |
| hypermagnesaemia | | |
| alternative dictionary used: MedDRA 26.0 | | |
| subjects affected / exposed | 1 / 265 (0.38%) | 1 / 258 (0.39%) |
| occurrences (all) | 2 | 1 |
| vitamin d deficiency | | |
| alternative dictionary used: MedDRA 26.0 | | |

| | | | |
|-----------------------------|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 265 (0.38%) | 1 / 258 (0.39%) | |
| occurrences (all) | 1 | 1 | |

Notes:

[2] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: Gender specific events only occurring in male or female participants have had the number of participants At Risk adjusted accordingly.

[3] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: Gender specific events only occurring in male or female participants have had the number of participants At Risk adjusted accordingly.

[4] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: Gender specific events only occurring in male or female participants have had the number of participants At Risk adjusted accordingly.

[5] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: Gender specific events only occurring in male or female participants have had the number of participants At Risk adjusted accordingly.

[6] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: Gender specific events only occurring in male or female participants have had the number of participants At Risk adjusted accordingly.

[7] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: Gender specific events only occurring in male or female participants have had the number of participants At Risk adjusted accordingly.

[8] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: Gender specific events only occurring in male or female participants have had the number of participants At Risk adjusted accordingly.

[9] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: Gender specific events only occurring in male or female participants have had the number of participants At Risk adjusted accordingly.

[10] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: Gender specific events only occurring in male or female participants have had the number of participants At Risk adjusted accordingly.

[11] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: Gender specific events only occurring in male or female participants have had the number of participants At Risk adjusted accordingly.

[12] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: Gender specific events only occurring in male or female participants have had the number of participants At Risk adjusted accordingly.

[13] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: Gender specific events only occurring in male or female participants have had the number of participants At Risk adjusted accordingly.

[14] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: Gender specific events only occurring in male or female participants have had the number of participants At Risk adjusted accordingly.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported