# Clinical trial results:
# PREVAIL: A Multinational Phase 3, Randomized, Double-Blind, Placebo-Controlled Efficacy and Safety Study of Oral MDV3100 in Chemotherapy-Naive Patients with Progressive Metastatic Prostate Cancer Who Have Failed Androgen Deprivation Therapy

## Summary

| | |
|---|---|
| EudraCT number | 2010-020821-41 |
| Trial protocol | DE BE GB NL ES SE AT FI DK SK IT LT |
| Global end of trial date | |

**Results information**

| | |
|---|---|
| Result version number | v1 |
| This version publication date | 20 October 2016 |
| First version publication date | 18 July 2015 |

## Trial information

**Trial identification**

| | |
|---|---|
| Sponsor protocol code | MDV3100-03 |

**Additional study identifiers**

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01212991 |
| WHO universal trial number (UTN) | - |

Notes:

**Sponsors**

| | |
|---|---|
| Sponsor organisation name | Medivation, Inc. |
| Sponsor organisation address | 525 Market St., San Francisco, United States, 94105 |
| Public contact | Phillip Cole, MD, Medivation, Inc., phillip.cole@medivation.com |
| Scientific contact | Phillip Cole, MD, Medivation, Inc., phillip.cole@medivation.com |

Notes:

**Paediatric regulatory details**

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

Notes:

## Results analysis stage

| | |
|---|---|
| Analysis stage | Interim |
| Date of interim/final analysis | 16 September 2013 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 16 September 2013 |
| Global end of trial reached? | No |

Notes:

## General information about the trial

Main objective of the trial:

The purpose of this study was to determine the benefit of enzalutamide versus placebo as assessed by overall survival and radiographic progression-free survival in patients with progressive metastatic prostate cancer who have failed androgen deprivation therapy and had not yet received cytotoxic chemotherapy.

Protection of trial subjects:

This study was conducted in conformance with the principles of the Declaration of Helsinki or with the laws and regulations of the country in which the research was conducted, whichever provided greater protection of the individual. In addition, the study was conducted using Good Clinical Practice (GCP) according to International Conference on Harmonisation (ICH) guidelines. Specifically, this study was based on adequately performed laboratory and animal experimentation; the study was conducted under a protocol reviewed and approved by an IRB/IEC; the study was conducted by scientifically and medically qualified persons; the benefits of the study were in proportion to the risks; the rights and welfare of the patients were respected; the physicians conducting the study did not find the hazards to outweigh the potential benefits.

Background therapy: -

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 28 September 2010 |
| Long term follow-up planned | Yes |
| Long term follow-up rationale | Safety, Efficacy |
| Long term follow-up duration | 5 Years |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

## Population of trial subjects

### Subjects enrolled per country

| | |
|---|---|
| Country: Number of subjects enrolled | United States: 247 |
| Country: Number of subjects enrolled | Slovakia: 27 |
| Country: Number of subjects enrolled | Finland: 33 |
| Country: Number of subjects enrolled | Spain: 81 |
| Country: Number of subjects enrolled | Lithuania: 14 |
| Country: Number of subjects enrolled | Austria: 18 |
| Country: Number of subjects enrolled | Israel: 25 |
| Country: Number of subjects enrolled | Russian Federation: 22 |
| Country: Number of subjects enrolled | United Kingdom: 153 |
| Country: Number of subjects enrolled | Italy: 30 |
| Country: Number of subjects enrolled | France: 175 |
| Country: Number of subjects enrolled | Canada: 179 |
| Country: Number of subjects enrolled | Poland: 39 |
| Country: Number of subjects enrolled | Belgium: 57 |

| | |
|---|---|
| Country: Number of subjects enrolled | Singapore: 9 |
| Country: Number of subjects enrolled | Australia: 232 |
| Country: Number of subjects enrolled | Denmark: 87 |
| Country: Number of subjects enrolled | Netherlands: 28 |
| Country: Number of subjects enrolled | Germany: 83 |
| Country: Number of subjects enrolled | Japan: 61 |
| Country: Number of subjects enrolled | Sweden: 39 |
| Country: Number of subjects enrolled | Korea, Republic of: 78 |
| Worldwide total number of subjects | 1717 |
| EEA total number of subjects | 864 |

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) | 358 |
| From 65 to 84 years | 1264 |
| 85 years and over | 95 |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

Patients were randomized 1:1 to receive either enzalutamide or placebo.

### 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** | Enzalutamide |

Arm description:

Patients received enzalutamide 160 mg, administered as four 40-mg capsules, once per day by mouth.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Enzalutamide |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

Patients received enzalutamide 160 mg, administered as four 40-mg capsules, once per day by mouth.

| | |
|---|---|
| **Arm title** | Placebo |

Arm description:

Patients received placebo, administered as four capsules, once per day by mouth.

| | |
|---|---|
| Arm type | Placebo |
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

Patients received placebo, administered as four capsules, once per day by mouth.

| **Number of subjects in period 1** | Enzalutamide | Placebo |
|---|---|---|
| Started | 872 | 845 |
| Completed | 259 | 471 |
| Not completed | 613 | 374 |
| Consent withdrawn by subject | 4 | 14 |
| Death | 241 | 299 |

| | | |
|---|---|---|
| Continuing Treatment | 367 | 61 |
| Lost to follow-up | 1 | - |

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | Enzalutamide |
| Reporting group description: | |
| Patients received enzalutamide 160 mg, administered as four 40-mg capsules, once per day by mouth. | |
| Reporting group title | Placebo |
| Reporting group description: | |
| Patients received placebo, administered as four capsules, once per day by mouth. | |

| Reporting group values | Enzalutamide | Placebo | Total |
|---|---|---|---|
| Number of subjects | 872 | 845 | 1717 |
| Age Categorical<br>Units: participants | | | |
| <=18 years | 0 | 0 | 0 |
| Between 18 and 65 years | 179 | 179 | 358 |
| >=65 years | 693 | 666 | 1359 |
| Age Continuous<br>Units: years | | | |
| arithmetic mean | 71.3 | 71.2 | |
| standard deviation | ± 8.51 | ± 8.42 | - |
| Gender, Male/Female<br>Units: participants | | | |
| Male | 872 | 845 | 1717 |
| Region of Enrollment<br>Units: Subjects | | | |
| United States | 127 | 120 | 247 |
| Slovakia | 13 | 14 | 27 |
| Finland | 18 | 15 | 33 |
| Spain | 44 | 37 | 81 |
| Lithuania | 8 | 6 | 14 |
| Austria | 9 | 9 | 18 |
| Russian Federation | 12 | 10 | 22 |
| Israel | 14 | 11 | 25 |
| United Kingdom | 78 | 75 | 153 |
| Italy | 15 | 15 | 30 |
| France | 85 | 90 | 175 |
| Canada | 91 | 88 | 179 |
| Poland | 21 | 18 | 39 |
| Belgium | 28 | 29 | 57 |
| Singapore | 5 | 4 | 9 |
| Australia | 116 | 116 | 232 |
| Denmark | 43 | 44 | 87 |
| Netherlands | 15 | 13 | 28 |
| Germany | 41 | 42 | 83 |
| Japan | 28 | 33 | 61 |
| Sweden | 21 | 18 | 39 |
| Korea, Republic of | 40 | 38 | 78 |

## End points

### End points reporting groups

| | |
|---|---|
| Reporting group title | Enzalutamide |
| Reporting group description: | |
| Patients received enzalutamide 160 mg, administered as four 40-mg capsules, once per day by mouth. | |
| Reporting group title | Placebo |
| Reporting group description: | |
| Patients received placebo, administered as four capsules, once per day by mouth. | |
| Subject analysis set title | Intent-to-treat: Radiographic Progression-free Survival |
| Subject analysis set type | Modified intention-to-treat |
| Subject analysis set description: | |
| All patients randomly assigned to treatment excluding 84 patients who were not randomized before the radiographic progression-free survival data cutoff date of 06 May 2012. | |
| Subject analysis set title | Evaluable Intent-to-treat Population |
| Subject analysis set type | Modified intention-to-treat |
| Subject analysis set description: | |
| All patients randomly assigned to treatment with PSA values at baseline and at least one postbaseline assessment. | |
| Subject analysis set title | Intent-to-treat With Measurable Disease |
| Subject analysis set type | Modified intention-to-treat |
| Subject analysis set description: | |
| All participants who were randomly assigned to treatment and had at least one target lesion at screening. | |
| Subject analysis set title | Intent-to-treat |
| Subject analysis set type | Intention-to-treat |
| Subject analysis set description: | |
| All patients randomly assigned to treatment. | |

### Primary: Overall Survival

| | |
|---|---|
| End point title | Overall Survival |
| End point description: | |
| Overall survival was defined as the time from randomization to death due to any cause. For patients who were alive at the time of the analysis data cutoff, overall survival was censored at the last date the patient was known to be alive or analysis data cutoff date, whichever was first. This included patients who were known to have died after the data analysis cutoff date. Patients with no post-baseline survival information were censored on the date of randomization.<br><br>'99999' indicates that the upper limit of the 95% confidence interval was not calculable because an insufficient number of patients reached the event at the final time point for assessment. | |
| End point type | Primary |
| End point timeframe: | |
| During study period (up to 3 years) | |

| End point values | Enzalutamide | Placebo | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 872[1] | 845[2] | | |
| Units: months | | | | |
| median (confidence interval 95%) | 32.4 (30.1 to 99999) | 30.2 (28 to 99999) | | |

Notes:

[1] - Intent-to-treat

[2] - Intent-to-treat

## Statistical analyses

| Statistical analysis title | Overall Survival |
|---|---|
| Comparison groups | Enzalutamide v Placebo |
| Number of subjects included in analysis | 1717 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 [3] |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.706 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.596 |
| upper limit | 0.837 |

Notes:

[3] - A 2-stage group-sequential method (Lan DeMets OBF) assigned the level of significance for the pre-specified interim overall survival analysis (p<0.015) based on overall 2-sided type I error rate of 0.049. Final results based upon interim analysis.

## Primary: Radiographic Progression-free Survival

| End point title | Radiographic Progression-free Survival |
|---|---|

End point description:

Radiographic progression-free survival (rPFS) was defined as the time from randomization to the first objective evidence of radiographic disease progression (rDP) assessed by blinded independent central radiology review or death due to any cause within 168 days after treatment discontinuation, whichever was first. RDP was evaluated by CT scan or MRI and radionuclide bone scans at regularly scheduled visits. RDP in bone required a confirmatory scan. RDP in soft tissue did not require a confirmatory scan for purposes of analysis. RDP was evaluated using RECIST 1.1 for soft tissue disease and PCWG2 guidelines for bone disease. Patients who did not reach the endpoint were censored at their last assessment.

'99999' indicates the median time to rPFS and its upper 95% confidence limit were not yet reached in the enzalutamide group because an insufficient number of patients had an event at the time of analysis.

| End point type | Primary |
|---|---|

End point timeframe:

During study period (up to 20 months)

| End point values | Enzalutamide | Placebo | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 832[4] | 801[5] | | |
| Units: months | | | | |
| median (confidence interval 95%) | 99999 (13.8 to 99999) | 3.9 (3.7 to 5.4) | | |

Notes:

[4] - Intent-to-treat: Radiographic Progression-free Survival

[5] - Intent-to-treat: Radiographic Progression-free Survival

### Statistical analyses

| **Statistical analysis title** | Radiographic Progression-free Survival |
|---|---|
| Comparison groups | Placebo v Enzalutamide |
| Number of subjects included in analysis | 1633 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 [6] |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.186 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.149 |
| upper limit | 0.231 |

Notes:

[6] - The assigned 2-sided type I error rate was 0.001 for the analysis of radiographic progression-free survival.

### Secondary: Time to First Skeletal-related Event

| End point title | Time to First Skeletal-related Event |
|---|---|

End point description:

Time to first skeletal-related event (SRE) was defined as the time from randomization to the date of the first occurrence of an SRE for each patient. An SRE was defined as radiation therapy or surgery to bone for prostate cancer, pathological bone fracture, spinal cord compression, or initiation/change in antineoplastic therapy to treat bone pain from prostate cancer. SREs were recorded at each scheduled and unscheduled study visit and during long-term follow-up if an SRE was not documented previously. Patients who did not have an SRE at the time of the analysis data cutoff were censored at the date of last assessment indicating no evidence of SRE. Patients with no postbaseline assessments were censored on the date of randomization.

'99999' indicates that the upper limit of the 95% confidence interval was not calculable because an insufficient number of patients reached the event at the final time point for assessment.

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

End point timeframe:

During study period (up to 3 years)

| **End point values** | Enzalutamide | Placebo | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 872[7] | 845[8] | | |
| Units: months | | | | |
| median (confidence interval 95%) | 31.1 (29.5 to 99999) | 31.3 (23.9 to 99999) | | |

Notes:

[7] - Intent-to-treat

[8] - Intent-to-treat

### Statistical analyses

| Statistical analysis title | Time to First Skeletal-related Event |
|---|---|
| Comparison groups | Enzalutamide v Placebo |
| Number of subjects included in analysis | 1717 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 [9] |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.718 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.61 |
| upper limit | 0.844 |

Notes:

[9] - The Holm step down method of multiple comparisons was used to maintain a study-wide type I error of 5% for prespecified secondary efficacy analyses. The 2-sided type I error rate was 0.01 for this analysis.

### Secondary: Time to Initiation of Cytotoxic Chemotherapy

| End point title | Time to Initiation of Cytotoxic Chemotherapy |
|---|---|

End point description:

The time to initiation of cytotoxic chemotherapy was defined as the time from randomization to the date of initiation of cytotoxic chemotherapy for the treatment of prostate cancer for each patient. For patients who did not start cytotoxic chemotherapy at the time of the analysis data cutoff, time to initiation of cytotoxic chemotherapy was censored at the date of last assessment where no cytotoxic chemotherapy was indicated or at the analysis data cutoff date, whichever was first. Time to initiation of cytotoxic chemotherapy for patients with no postbaseline assessments was censored on the date of randomization.

'99999' indicates that the upper limit of the 95% confidence interval was not calculable because an insufficient number of patients in the enzalutamide group reached the event at the final time point for assessment.

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

End point timeframe:

During study period (up to 3 years)

| End point values | Enzalutamide | Placebo | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 872[10] | 845[11] | | |
| Units: months | | | | |
| median (confidence interval 95%) | 28 (25.8 to 99999) | 10.8 (9.7 to 12.2) | | |

Notes:

[10] - Intent-to-treat

[11] - Intent-to-treat

### Statistical analyses

| Statistical analysis title | Time to Initiation of Cytotoxic Chemotherapy |
|---|---|
| Comparison groups | Enzalutamide v Placebo |
| Number of subjects included in analysis | 1717 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 [12] |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.349 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.303 |
| upper limit | 0.403 |

Notes:

[12] - The Holm step down method of multiple comparisons was used to maintain a study wide type I error of 5% for prespecified secondary efficacy analyses. The 2-sided type I error rate was 0.0125 for this analysis.

### Secondary: Time to Prostate-specific Antigen (PSA) Progression

| End point title | Time to Prostate-specific Antigen (PSA) Progression |
|---|---|

End point description:

Time to PSA progression was defined as the time from randomization to date of first confirmed observation of PSA progression for each patient. For patients with PSA declines at week 13, the PSA progression date was defined as the date that a ≥ 25% increase and an absolute increase of ≥ 2 ng/mL above the nadir was documented, and confirmed 3 or more weeks later. For patients with no PSA decline at week 13, the PSA progression date was defined as the date that a ≥ 25% increase and an absolute increase of ≥ 2 ng/mL above baseline was documented, and confirmed 3 or more weeks later. For patients who did not have confirmed PSA progression at the time of the analysis data cutoff, time to PSA progression was censored at the date of the last PSA assessment showing no evidence of confirmed PSA progression or the analysis data cutoff date, whichever was first. Time to PSA progression for patients with no postbaseline assessments was censored on the date of randomization.

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

End point timeframe:

During study period (up to 3 years)

| End point values | Enzalutamide | Placebo | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 872[13] | 845[14] | | |
| Units: months | | | | |
| median (confidence interval 95%) | 11.2 (11.1 to 13.7) | 2.8 (2.8 to 2.9) | | |

Notes:

[13] - Intent-to-treat

[14] - Intent-to-treat

### Statistical analyses

| Statistical analysis title | Time to PSA Progression |
|---|---|
| Comparison groups | Enzalutamide v Placebo |
| Number of subjects included in analysis | 1717 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 [15] |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.169 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.147 |
| upper limit | 0.195 |

Notes:

[15] - The Holm step down method of multiple comparisons was used to maintain a study wide type I error of 5% for prespecified secondary efficacy analyses. The 2-sided type I error rate was 0.0167 for this analysis.

### Secondary: Percentage of Patients With Prostate Specific Antigen (PSA) Response ≥ 50%

| End point title | Percentage of Patients With Prostate Specific Antigen (PSA) Response ≥ 50% |
|---|---|

End point description:

PSA response was defined as a ≥ 50% reduction in PSA from baseline to the lowest postbaseline PSA value and required confirmation by a consecutive assessment at least 3 weeks later. Patients were evaluable for PSA response rate if a patient had a PSA level measured at baseline and at least one postbaseline assessment.

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

End point timeframe:

During study period (up to 3 years)

| End point values | Enzalutamide | Placebo | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 854[16] | 777[17] | | |
| Units: Percentage of Participants | | | | |
| number (confidence interval 95%) | 78 (75.1 to 80.7) | 3.5 (2.3 to 5) | | |

Notes:

[16] - Evaluable Intent-to-treat Population

[17] - Evaluable Intent-to-treat Population

### Statistical analyses

| Statistical analysis title | Percentage of Patients With PSA Response ≥ 50% |
|---|---|
| Comparison groups | Enzalutamide v Placebo |
| Number of subjects included in analysis | 1631 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 [18] |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Difference in response rates |
| Point estimate | 74.51 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 71.45 |
| upper limit | 77.57 |

Notes:

[18] - The Holm step down method of multiple comparisons was used to maintain a study wide type I error of 5% for prespecified secondary efficacy analyses. The 2-sided type I error rate was 0.025 for this analysis.

## Secondary: Best Overall Soft Tissue Response

| End point title | Best Overall Soft Tissue Response |
|---|---|

End point description:

The best overall soft tissue objective response was defined as partial response [PR] or complete response [CR] while on study treatment based on investigator assessments of target, nontarget, and new lesions using RECIST 1.1. Soft tissue was assessed by CT or MRI at regularly scheduled visits. Only patients with measurable soft tissue disease (ie, at least 1 target lesion identified per RECIST 1.1) at screening are included in this analysis. All percentages are based on number of patients with measurable soft tissue disease at screening in each treatment group.

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

End point timeframe:

During study period (up to 3 years)

| End point values | Enzalutamide | Placebo | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 396[19] | 381[20] | | |
| Units: Percentage of participants | | | | |
| number (not applicable) | 58.8 | 5 | | |

Notes:

[19] - Intent-to-treat With Measurable Disease

[20] - Intent-to-treat With Measurable Disease

### Statistical analyses

| **Statistical analysis title** | Best Overall Soft Tissue Response |
|---|---|
| Comparison groups | Enzalutamide v Placebo |
| Number of subjects included in analysis | 777 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 [21] |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Difference in objective response rate |
| Point estimate | 53.85 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 48.53 |
| upper limit | 59.17 |

Notes:

[21] - The Holm step down method of multiple comparisons was used to maintain a study wide type I error of 5% for prespecified secondary efficacy analyses. The 2-sided type I error rate was 0.05 for this analysis.

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

The period of time from the date of the first dose of study drug to 28 days after last dose of study drug or 1 day before the date of initiation of cytotoxic chemotherapy or an investigational agent for prostate cancer, whichever was first.

Adverse event reporting additional description:

Safety population (patients at risk) was defined as patients that received at least 1 dose of study drug. 1717 patients were randomly assigned 1:1 to treatment with enzalutamide (872 patients) or placebo (845 patients), however only 1715 patients received at least 1 dose of enzalutamide (871 patients) or placebo (844 patients).

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

### Dictionary used

| | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 16.1 |

### Reporting groups

| | |
|---|---|
| Reporting group title | Enzalutamide |

Reporting group description:

Patients received enzalutamide 160 mg, administered as four 40-mg capsules, once per day by mouth.

| | |
|---|---|
| Reporting group title | Placebo |

Reporting group description:

Patients received placebo, administered as four capsules, once per day by mouth.

| Serious adverse events | Enzalutamide | Placebo | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 279 / 871 (32.03%) | 226 / 844 (26.78%) | |
| number of deaths (all causes) | 241 | 299 | |
| number of deaths resulting from adverse events | | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Metastatic pain | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 17 / 871 (1.95%) | 17 / 844 (2.01%) | |
| occurrences causally related to treatment / all | 0 / 20 | 0 / 20 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cancer pain | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 3 / 871 (0.34%) | 3 / 844 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastric cancer | | | |

| | | | |
|---|---|---|---|
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 2 / 871 (0.23%) | 1 / 844 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Transitional cell carcinoma | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 3 / 871 (0.34%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Adenocarcinoma of colon | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 2 / 871 (0.23%) | 1 / 844 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lung adenocarcinoma | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 1 / 844 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Malignant pleural effusion | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 1 / 844 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metastases to central nervous system | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 1 / 844 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metastases to liver | | | |
| alternative dictionary used: MedDRA 16.1 | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 871 (0.00%) | 2 / 844 (0.24%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metastases to meninges | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 1 / 844 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metastases to soft tissue | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 1 / 844 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metastases to spine | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 2 / 871 (0.23%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Prostate cancer metastatic | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 871 (0.00%) | 2 / 844 (0.24%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 2 | |
| Rectal cancer | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 2 / 871 (0.23%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Malignant melanoma | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 2 / 871 (0.23%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|---|---|---|
| Prostate cancer | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 1 / 844 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Tonsil cancer | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 2 / 871 (0.23%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Adenocarcinoma gastric | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Anal cancer | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 871 (0.00%) | 1 / 844 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bladder cancer | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bladder transitional cell carcinoma | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Colon cancer | | | |
| alternative dictionary used: MedDRA 16.1 | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 871 (0.11%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Colorectal cancer | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatocellular carcinoma | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Intestinal adenocarcinoma | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lung neoplasm malignant | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metastases to bladder | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metastases to bone | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|---|---|---|
| Metastases to bone marrow | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metastases to breast | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metastases to lung | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 871 (0.00%) | 1 / 844 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metastases to peritoneum | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Neuroendocrine carcinoma of the skin | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 871 (0.00%) | 1 / 844 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Osteosarcoma | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal cell carcinoma | | | |
| alternative dictionary used: MedDRA 16.1 | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 871 (0.11%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Small cell lung cancer limited stage | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Thyroid adenoma | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Tumour associated fever | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 871 (0.00%) | 1 / 844 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Tumour embolism | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 871 (0.00%) | 1 / 844 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 1 / 1 | |
| Tumour pain | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| B-cell lymphoma | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|---|---|---|
| Gastrointestinal stromal tumour | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Myelodysplastic syndrome | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 871 (0.00%) | 1 / 844 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vascular disorders | | | |
| Deep vein thrombosis | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 4 / 871 (0.46%) | 2 / 844 (0.24%) | |
| occurrences causally related to treatment / all | 0 / 5 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypertension | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 4 / 871 (0.46%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 2 / 4 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypotension | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 1 / 844 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Orthostatic hypotension | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 1 / 844 (0.12%) | |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Aortic aneurysm | | | |
| alternative dictionary used: MedDRA 16.1 | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 871 (0.00%) | 1 / 844 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Aortic aneurysm rupture | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Circulatory collapse | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Hypovolaemic shock | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lymphoedema | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vena cava thrombosis | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 871 (0.00%) | 1 / 844 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Aortic stenosis | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|---|---|---|
| Phlebitis | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 871 (0.00%) | 1 / 844 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Subclavian artery stenosis | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| **Surgical and medical procedures** | | | |
| Cancer hormonal therapy | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pain management | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 871 (0.00%) | 1 / 844 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| **General disorders and administration site conditions** | | | |
| General physical health deterioration | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 14 / 871 (1.61%) | 10 / 844 (1.18%) | |
| occurrences causally related to treatment / all | 0 / 14 | 0 / 10 | |
| deaths causally related to treatment / all | 0 / 9 | 0 / 4 | |
| Disease progression | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 3 / 871 (0.34%) | 7 / 844 (0.83%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 7 | |
| deaths causally related to treatment / all | 0 / 3 | 0 / 6 | |
| Death | | | |

| | | | |
|---|---|---|---|
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 4 / 871 (0.46%) | 1 / 844 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 4 | 0 / 1 | |
| Oedema peripheral | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 3 / 844 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Fatigue | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 4 / 871 (0.46%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 4 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gait disturbance | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 1 / 844 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pain | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 2 / 871 (0.23%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Performance status decreased | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 871 (0.00%) | 2 / 844 (0.24%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Pyrexia | | | |
| alternative dictionary used: MedDRA 16.1 | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 871 (0.11%) | 1 / 844 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Asthenia | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 871 (0.00%) | 1 / 844 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Chest pain | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Device dislocation | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 871 (0.00%) | 1 / 844 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Drowning | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Generalised oedema | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Medical device complication | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 871 (0.00%) | 1 / 844 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|---|---|---|
| Non-cardiac chest pain | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Oedema | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sudden death | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 871 (0.00%) | 1 / 844 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Suprapubic pain | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 871 (0.00%) | 1 / 844 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Adverse drug reaction | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Device occlusion | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 871 (0.00%) | 1 / 844 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Local swelling | | | |
| alternative dictionary used: MedDRA 16.1 | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 871 (0.11%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Immune system disorders | | | |
| Anaphylactic shock | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 871 (0.00%) | 1 / 844 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Drug hypersensitivity | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Reproductive system and breast disorders | | | |
| Benign prostatic hyperplasia | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 871 (0.00%) | 1 / 844 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pelvic pain | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Prostatic obstruction | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Prostatitis | | | |
| alternative dictionary used: MedDRA 16.1 | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 871 (0.11%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Testicular pain | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| **Respiratory, thoracic and mediastinal disorders** | | | |
| Pulmonary embolism | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 5 / 871 (0.57%) | 7 / 844 (0.83%) | |
| occurrences causally related to treatment / all | 0 / 5 | 3 / 7 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Chronic obstructive pulmonary disease | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 3 / 871 (0.34%) | 3 / 844 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 5 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Dyspnoea | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 3 / 871 (0.34%) | 2 / 844 (0.24%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumothorax | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 2 / 871 (0.23%) | 1 / 844 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pleural effusion | | | |
| alternative dictionary used: MedDRA 16.1 | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 871 (0.11%) | 1 / 844 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Epistaxis | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 1 / 844 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Acute pulmonary oedema | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Aspiration | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Asthma | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 871 (0.00%) | 1 / 844 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haemothorax | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hydrothorax | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|---|---|---|
| Hypoxia | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 871 (0.00%) | 1 / 844 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nasal polyps | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Organising pneumonia | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia aspiration | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonitis | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pulmonary haemorrhage | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 871 (0.00%) | 1 / 844 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 1 / 1 | |
| Restrictive pulmonary disease | | | |
| alternative dictionary used: MedDRA 16.1 | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 871 (0.00%) | 1 / 844 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Tracheal obstruction extrinsic | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Psychiatric disorders | | | |
| Confusional state | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 4 / 844 (0.47%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Suicide attempt | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 1 / 844 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Depression | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 871 (0.00%) | 1 / 844 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Major depression | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 871 (0.00%) | 1 / 844 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Investigations | | | |
| Electrocardiogram QT prolonged | | | |
| alternative dictionary used: MedDRA 16.1 | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 871 (0.11%) | 1 / 844 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haemoglobin decreased | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 2 / 871 (0.23%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Platelet count decreased | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 1 / 844 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatic enzyme increased | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 871 (0.00%) | 2 / 844 (0.24%) | |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Arteriogram coronary | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 871 (0.00%) | 1 / 844 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Blood creatinine increased | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 871 (0.00%) | 1 / 844 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Coagulation time prolonged | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|---|---|---|
| Eastern cooperative oncology group performance status worsened | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 871 (0.00%) | 1 / 844 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| International normalised ratio increased | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 871 (0.00%) | 1 / 844 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Electrocardiogram repolarisation abnormality | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Weight decreased | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| **Injury, poisoning and procedural complications** | | | |
| Fall | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 7 / 871 (0.80%) | 3 / 844 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 7 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Femoral neck fracture | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 5 / 871 (0.57%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 6 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Femur fracture | | | |

| | | | |
|---|---|---|---|
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 3 / 871 (0.34%) | 2 / 844 (0.24%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Spinal compression fracture | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 3 / 871 (0.34%) | 1 / 844 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Road traffic accident | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 2 / 871 (0.23%) | 1 / 844 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Humerus fracture | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 3 / 871 (0.34%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Wrist fracture | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 3 / 871 (0.34%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hip fracture | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 871 (0.00%) | 2 / 844 (0.24%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Subdural haematoma | | | |
| alternative dictionary used: MedDRA 16.1 | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 871 (0.00%) | 2 / 844 (0.24%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Toxicity to various agents | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 2 / 871 (0.23%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cystitis radiation | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 2 / 871 (0.23%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ankle fracture | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 871 (0.00%) | 1 / 844 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Chest injury | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 871 (0.00%) | 1 / 844 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Clavicle fracture | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Extradural haematoma | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|---|---|---|
| Facial bones fracture | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Foreign body | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastroenteritis radiation | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hand fracture | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 871 (0.00%) | 1 / 844 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Head injury | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lumbar vertebral fracture | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 871 (0.00%) | 1 / 844 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Post procedural haemorrhage | | | |
| alternative dictionary used: MedDRA 16.1 | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 871 (0.00%) | 1 / 844 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Radiation oesophagitis | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 871 (0.00%) | 1 / 844 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Radius fracture | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Skeletal injury | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Subdural haemorrhage | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Tibia fracture | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 871 (0.00%) | 1 / 844 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Traumatic fracture | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|---|---|---|
| Traumatic intracranial haemorrhage<br>alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Upper limb fracture<br>alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Contrast media reaction<br>alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Contusion<br>alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lower limb fracture<br>alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Post procedural haematuria<br>alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 871 (0.00%) | 1 / 844 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Procedural pain<br>alternative dictionary used: MedDRA 16.1 | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 871 (0.11%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pubis fracture | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 871 (0.00%) | 1 / 844 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vascular pseudoaneurysm | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| **Cardiac disorders** | | | |
| Atrial fibrillation | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 6 / 871 (0.69%) | 6 / 844 (0.71%) | |
| occurrences causally related to treatment / all | 2 / 7 | 2 / 6 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac failure | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 3 / 871 (0.34%) | 2 / 844 (0.24%) | |
| occurrences causally related to treatment / all | 1 / 4 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 2 | 0 / 0 | |
| Cardiac arrest | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 2 / 871 (0.23%) | 2 / 844 (0.24%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 2 | 0 / 1 | |
| Myocardial infarction | | | |
| alternative dictionary used: MedDRA 16.1 | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 3 / 871 (0.34%) | 1 / 844 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Coronary artery disease | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 4 / 871 (0.46%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Acute myocardial infarction | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 3 / 871 (0.34%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 2 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Arteriosclerosis coronary artery | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 1 / 844 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 1 | |
| Atrioventricular block | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 1 / 844 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Acute coronary syndrome | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Angina pectoris | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|---|---|---|
| Angina unstable | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 871 (0.00%) | 1 / 844 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac failure acute | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 871 (0.00%) | 1 / 844 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac failure congestive | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 871 (0.00%) | 1 / 844 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Cardiopulmonary failure | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Congestive cardiomyopathy | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypertensive heart disease | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sick sinus syndrome | | | |
| alternative dictionary used: MedDRA 16.1 | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 871 (0.00%) | 1 / 844 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sinus tachycardia | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 871 (0.00%) | 1 / 844 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Supraventricular tachycardia | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ventricular tachycardia | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 871 (0.00%) | 1 / 844 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ventricular extrasystoles | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| **Nervous system disorders** | | | |
| Spinal cord compression | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 28 / 871 (3.21%) | 24 / 844 (2.84%) | |
| occurrences causally related to treatment / all | 0 / 29 | 0 / 24 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Syncope | | | |
| alternative dictionary used: MedDRA 16.1 | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 6 / 871 (0.69%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 6 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cerebrovascular accident | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 4 / 871 (0.46%) | 1 / 844 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 2 | 0 / 0 | |
| Cauda equina syndrome | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 4 / 871 (0.46%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nerve root compression | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 2 / 871 (0.23%) | 2 / 844 (0.24%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Transient ischaemic attack | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 2 / 871 (0.23%) | 3 / 844 (0.36%) | |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Presyncope | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 3 / 871 (0.34%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Paraesthesia | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 871 (0.00%) | 2 / 844 (0.24%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|---|---|---|
| Paraparesis | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 1 / 844 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ataxia | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Brain injury | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 871 (0.00%) | 1 / 844 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Cerebral haemorrhage | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 871 (0.00%) | 1 / 844 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cerebral infarction | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cervicobrachial syndrome | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Coma hepatic | | | |
| alternative dictionary used: MedDRA 16.1 | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 871 (0.00%) | 1 / 844 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Dementia | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 871 (0.00%) | 1 / 844 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lethargy | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 871 (0.00%) | 1 / 844 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Memory impairment | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 871 (0.00%) | 1 / 844 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Meningorrhagia | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metabolic encephalopathy | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 871 (0.00%) | 1 / 844 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Reversible ischaemic neurological deficit | | | |
| alternative dictionary used: MedDRA 16.1 | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 871 (0.00%) | 1 / 844 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Spinal cord ischaemia | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 0 / 844 (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 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vith nerve disorder | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 871 (0.00%) | 1 / 844 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Complex partial seizures | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 871 (0.00%) | 1 / 844 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Neuralgia | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sciatica | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 871 (0.00%) | 1 / 844 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|---|---|---|
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 14 / 871 (1.61%) | 8 / 844 (0.95%) | |
| occurrences causally related to treatment / all | 1 / 19 | 0 / 11 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Disseminated intravascular coagulation | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 1 / 844 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Iron deficiency anaemia | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Neutropenia | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pancytopenia | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ear and labyrinth disorders | | | |
| Vertigo | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Eye disorders | | | |

| | | | |
|---|---|---|---|
| Amaurosis | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 871 (0.00%) | 1 / 844 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cataract | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Retinal artery occlusion | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| Constipation | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 4 / 871 (0.46%) | 5 / 844 (0.59%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 6 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vomiting | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 2 / 871 (0.23%) | 2 / 844 (0.24%) | |
| occurrences causally related to treatment / all | 0 / 2 | 2 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diarrhoea | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 3 / 871 (0.34%) | 1 / 844 (0.12%) | |
| occurrences causally related to treatment / all | 2 / 3 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nausea | | | |
| alternative dictionary used: MedDRA 16.1 | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 3 / 871 (0.34%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Upper gastrointestinal haemorrhage | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 3 / 871 (0.34%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Abdominal pain | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 1 / 844 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal haemorrhage | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 1 / 844 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Inguinal hernia | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 1 / 844 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Intestinal obstruction | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 871 (0.00%) | 2 / 844 (0.24%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Melaena | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 1 / 844 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|---|---|---|
| Small intestinal obstruction<br>alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 1 / 844 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Duodenal ulcer haemorrhage<br>alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 2 / 871 (0.23%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Abdominal pain lower<br>alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diverticulum intestinal haemorrhagic<br>alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dysphagia<br>alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 871 (0.00%) | 1 / 844 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastric ulcer haemorrhage<br>alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Large intestinal haemorrhage<br>alternative dictionary used: MedDRA 16.1 | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 871 (0.00%) | 1 / 844 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Large intestine polyp | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lower gastrointestinal haemorrhage | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pancreatitis acute | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Peritoneal haemorrhage | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Rectal stenosis | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Subileus | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|---|---|---|
| Duodenal ulcer | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastritis | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatobiliary disorders | | | |
| Bile duct obstruction | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 871 (0.00%) | 1 / 844 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cholecystitis | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 871 (0.00%) | 1 / 844 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cholecystitis chronic | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 871 (0.00%) | 1 / 844 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatic failure | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Hepatic function abnormal | | | |
| alternative dictionary used: MedDRA 16.1 | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 871 (0.11%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Jaundice | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Jaundice cholestatic | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Skin and subcutaneous tissue disorders | | | |
| Toxic skin eruption | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 2 / 871 (0.23%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Rash | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Swelling face | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal and urinary disorders | | | |
| Urinary retention | | | |
| alternative dictionary used: MedDRA 16.1 | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 10 / 871 (1.15%) | 13 / 844 (1.54%) | |
| occurrences causally related to treatment / all | 0 / 13 | 0 / 13 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haematuria | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 5 / 871 (0.57%) | 12 / 844 (1.42%) | |
| occurrences causally related to treatment / all | 0 / 9 | 0 / 12 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urinary tract obstruction | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 7 / 871 (0.80%) | 8 / 844 (0.95%) | |
| occurrences causally related to treatment / all | 0 / 9 | 0 / 9 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hydronephrosis | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 871 (0.00%) | 11 / 844 (1.30%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 11 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Renal failure acute | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 5 / 871 (0.57%) | 5 / 844 (0.59%) | |
| occurrences causally related to treatment / all | 3 / 5 | 1 / 5 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 2 | |
| Ureteric obstruction | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 4 / 871 (0.46%) | 4 / 844 (0.47%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Obstructive uropathy | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 2 / 871 (0.23%) | 6 / 844 (0.71%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 7 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |

| | | | |
|---|---|---|---|
| Bladder outlet obstruction | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 2 / 871 (0.23%) | 3 / 844 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 5 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Postrenal failure | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 3 / 844 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 1 | 2 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Urinary bladder haemorrhage | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 3 / 871 (0.34%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Calculus bladder | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 1 / 844 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Prerenal failure | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 1 / 844 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal failure | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 1 / 844 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Acute prerenal failure | | | |
| alternative dictionary used: MedDRA 16.1 | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 871 (0.00%) | 1 / 844 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bladder obstruction | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 871 (0.00%) | 1 / 844 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nephrolithiasis | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal failure chronic | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urethral meatus stenosis | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 871 (0.00%) | 1 / 844 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urethral obstruction | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 871 (0.00%) | 1 / 844 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urine flow decreased | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|---|---|---|
| Bladder neck obstruction | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Micturition urgency | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 871 (0.00%) | 1 / 844 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Endocrine disorders | | | |
| Adrenal insufficiency | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 871 (0.00%) | 1 / 844 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Goitre | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Inappropriate antidiuretic hormone secretion | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal and connective tissue disorders | | | |
| Pathological Fracture | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 10 / 871 (1.15%) | 5 / 844 (0.59%) | |
| occurrences causally related to treatment / all | 0 / 10 | 0 / 5 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Back pain | | | |

| | | | |
|---|---|---|---|
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 4 / 871 (0.46%) | 5 / 844 (0.59%) | |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 5 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bone pain | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 3 / 871 (0.34%) | 5 / 844 (0.59%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 5 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Osteoarthritis | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 2 / 871 (0.23%) | 2 / 844 (0.24%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Intervertebral disc protrusion | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 2 / 871 (0.23%) | 1 / 844 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Muscular weakness | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 2 / 844 (0.24%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal chest pain | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 871 (0.00%) | 3 / 844 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Arthralgia | | | |
| alternative dictionary used: MedDRA 16.1 | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 2 / 871 (0.23%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Neck pain | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 871 (0.00%) | 2 / 844 (0.24%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Osteolysis | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 871 (0.00%) | 2 / 844 (0.24%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Spinal column stenosis | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 2 / 871 (0.23%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lumbar spinal stenosis | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 871 (0.00%) | 1 / 844 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal pain | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 0 / 844 (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 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | | |
|---|---|---|---|---|
| Myopathy | | | | |
| alternative dictionary used: MedDRA 16.1 | | | | |
| subjects affected / exposed | 0 / 871 (0.00%) | 1 / 844 (0.12%) | | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | | |
| Periostitis | | | | |
| alternative dictionary used: MedDRA 16.1 | | | | |
| subjects affected / exposed | 0 / 871 (0.00%) | 1 / 844 (0.12%) | | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | | |
| Rhabdomyolysis | | | | |
| alternative dictionary used: MedDRA 16.1 | | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 0 / 844 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | | |
| Spinal osteoarthritis | | | | |
| alternative dictionary used: MedDRA 16.1 | | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 0 / 844 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | | |
| Arthritis | | | | |
| alternative dictionary used: MedDRA 16.1 | | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 0 / 844 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | | |
| Groin pain | | | | |
| alternative dictionary used: MedDRA 16.1 | | | | |
| subjects affected / exposed | 0 / 871 (0.00%) | 1 / 844 (0.12%) | | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | | |
| Pain in extremity | | | | |
| alternative dictionary used: MedDRA 16.1 | | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 871 (0.00%) | 1 / 844 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Pneumonia | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 10 / 871 (1.15%) | 6 / 844 (0.71%) | |
| occurrences causally related to treatment / all | 0 / 13 | 0 / 6 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Urinary tract infection | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 6 / 871 (0.69%) | 5 / 844 (0.59%) | |
| occurrences causally related to treatment / all | 0 / 10 | 0 / 5 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urosepsis | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 5 / 871 (0.57%) | 3 / 844 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sepsis | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 4 / 844 (0.47%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastroenteritis | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 3 / 871 (0.34%) | 1 / 844 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 3 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Device related infection | | | |
| alternative dictionary used: MedDRA 16.1 | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 2 / 871 (0.23%) | 1 / 844 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bronchitis | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 1 / 844 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cellulitis | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 1 / 844 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infection | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 2 / 871 (0.23%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Herpes zoster | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 1 / 844 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Appendicitis | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 871 (0.00%) | 1 / 844 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Appendicitis perforated | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 0 / 844 (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 16.1 | | | |
| subjects affected / exposed | 0 / 871 (0.00%) | 1 / 844 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diverticulitis | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gallbladder abscess | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 871 (0.00%) | 1 / 844 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastroenteritis staphylococcal | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 0 / 844 (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 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Osteomyelitis | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 871 (0.00%) | 1 / 844 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Peritonitis | | | |
| alternative dictionary used: MedDRA 16.1 | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 871 (0.11%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory tract infection | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 871 (0.00%) | 1 / 844 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Septic shock | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 871 (0.00%) | 1 / 844 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Urinary tract infection fungal | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 871 (0.00%) | 1 / 844 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Viral infection | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 871 (0.00%) | 1 / 844 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Wound infection | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Chronic sinusitis | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|---|---|---|
| Metabolism and nutrition disorders | | | |
| Dehydration | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 3 / 844 (0.36%) | |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Decreased appetite | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 871 (0.00%) | 2 / 844 (0.24%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypercalcaemia | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 2 / 871 (0.23%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypoglycaemia | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 1 / 844 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cachexia | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 871 (0.00%) | 1 / 844 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Fluid retention | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 871 (0.00%) | 1 / 844 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hyperkalaemia | | | |
| alternative dictionary used: MedDRA 16.1 | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 871 (0.11%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypokalaemia | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hyponatraemia | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 0 / 871 (0.00%) | 1 / 844 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Type 2 diabetes mellitus | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metabolic acidosis | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 1 / 871 (0.11%) | 0 / 844 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

Frequency threshold for reporting non-serious adverse events: 5 %

| **Non-serious adverse events** | Enzalutamide | Placebo | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 844 / 871 (96.90%) | 787 / 844 (93.25%) | |
| Vascular disorders | | | |
| Hot flush | | | |
| alternative dictionary used: MedDRA 16.1 | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 157 / 871 (18.03%) | 65 / 844 (7.70%) | |
| occurrences (all) | 166 | 66 | |
| Hypertension | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 117 / 871 (13.43%) | 35 / 844 (4.15%) | |
| occurrences (all) | 158 | 41 | |
| General disorders and administration site conditions | | | |
| Fatigue | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 310 / 871 (35.59%) | 218 / 844 (25.83%) | |
| occurrences (all) | 404 | 262 | |
| Asthenia | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 113 / 871 (12.97%) | 67 / 844 (7.94%) | |
| occurrences (all) | 195 | 77 | |
| Oedema peripheral | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 92 / 871 (10.56%) | 69 / 844 (8.18%) | |
| occurrences (all) | 115 | 83 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 72 / 871 (8.27%) | 58 / 844 (6.87%) | |
| occurrences (all) | 82 | 62 | |
| Dyspnoea | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 69 / 871 (7.92%) | 60 / 844 (7.11%) | |
| occurrences (all) | 82 | 66 | |
| Psychiatric disorders | | | |
| Insomnia | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 70 / 871 (8.04%) | 47 / 844 (5.57%) | |
| occurrences (all) | 75 | 47 | |
| Investigations | | | |

| | | | |
|---|---|---|---|
| Weight decreased | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 100 / 871 (11.48%) | 71 / 844 (8.41%) | |
| occurrences (all) | 111 | 83 | |
| Injury, poisoning and procedural complications | | | |
| Fall | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 101 / 871 (11.60%) | 45 / 844 (5.33%) | |
| occurrences (all) | 129 | 48 | |
| Nervous system disorders | | | |
| Headache | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 91 / 871 (10.45%) | 59 / 844 (6.99%) | |
| occurrences (all) | 121 | 69 | |
| Dizziness | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 76 / 871 (8.73%) | 53 / 844 (6.28%) | |
| occurrences (all) | 87 | 58 | |
| Dysgeusia | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 66 / 871 (7.58%) | 31 / 844 (3.67%) | |
| occurrences (all) | 72 | 31 | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 66 / 871 (7.58%) | 69 / 844 (8.18%) | |
| occurrences (all) | 105 | 113 | |
| Gastrointestinal disorders | | | |
| Nausea | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 201 / 871 (23.08%) | 190 / 844 (22.51%) | |
| occurrences (all) | 253 | 217 | |
| Constipation | | | |
| alternative dictionary used: MedDRA 16.1 | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 193 / 871 (22.16%) | 145 / 844 (17.18%) | |
| occurrences (all) | 229 | 169 | |
| Diarrhoea | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 142 / 871 (16.30%) | 119 / 844 (14.10%) | |
| occurrences (all) | 187 | 155 | |
| Vomiting | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 59 / 871 (6.77%) | 70 / 844 (8.29%) | |
| occurrences (all) | 70 | 93 | |
| Abdominal pain | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 46 / 871 (5.28%) | 33 / 844 (3.91%) | |
| occurrences (all) | 50 | 47 | |
| Renal and urinary disorders | | | |
| Haematuria | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 73 / 871 (8.38%) | 49 / 844 (5.81%) | |
| occurrences (all) | 113 | 65 | |
| Pollakiuria | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 50 / 871 (5.74%) | 37 / 844 (4.38%) | |
| occurrences (all) | 58 | 40 | |
| Musculoskeletal and connective tissue disorders | | | |
| Back pain | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 235 / 871 (26.98%) | 187 / 844 (22.16%) | |
| occurrences (all) | 329 | 272 | |
| Arthralgia | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 177 / 871 (20.32%) | 135 / 844 (16.00%) | |
| occurrences (all) | 272 | 186 | |
| Pain in extremity | | | |
| alternative dictionary used: MedDRA 16.1 | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 102 / 871 (11.71%) | 97 / 844 (11.49%) | |
| occurrences (all) | 138 | 124 | |
| Bone pain | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 80 / 871 (9.18%) | 116 / 844 (13.74%) | |
| occurrences (all) | 102 | 142 | |
| Musculoskeletal pain | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 87 / 871 (9.99%) | 73 / 844 (8.65%) | |
| occurrences (all) | 108 | 89 | |
| Musculoskeletal chest pain | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 59 / 871 (6.77%) | 43 / 844 (5.09%) | |
| occurrences (all) | 69 | 53 | |
| Myalgia | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 52 / 871 (5.97%) | 49 / 844 (5.81%) | |
| occurrences (all) | 64 | 60 | |
| Infections and infestations | | | |
| Urinary tract infection | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 58 / 871 (6.66%) | 58 / 844 (6.87%) | |
| occurrences (all) | 82 | 73 | |
| Nasopharyngitis | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 62 / 871 (7.12%) | 42 / 844 (4.98%) | |
| occurrences (all) | 71 | 45 | |
| Upper respiratory tract infection | | | |
| alternative dictionary used: MedDRA 16.1 | | | |
| subjects affected / exposed | 53 / 871 (6.08%) | 30 / 844 (3.55%) | |
| occurrences (all) | 65 | 38 | |
| Metabolism and nutrition disorders | | | |
| Decreased appetite | | | |
| alternative dictionary used: MedDRA 16.1 | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed<br>occurrences (all) | 158 / 871 (18.14%)<br>190 | 136 / 844 (16.11%)<br>164 | |

## More information

## Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---|---|
| 27 August 2010 | The main purpose of this amendment was to specify that there would be a formal interim analysis and a primary analysis for overall survival. The primary analysis of overall survival would be performed when at least a total of 888 deaths were reported. Furthermore, it was specified that an unstratified log-rank test would be used to compare the MDV3100-treated and the placebo groups for both the interim and final analyses. Additionally, this amendment stipulated that the study would not be discontinued based upon the primary analysis of progression-free survival but rather the trial would continue until the primary analysis of the overall survival co-primary endpoint was completed. |
| 23 July 2012 | The main purpose of this amendment was to uncouple the interim analysis of progression-free survival from the completion of enrollment, which proceeded more quickly than expected. In addition, information on potential drug-drug interactions was updated based on completed clinical trials. |
| 14 March 2013 | The main purpose of this amendment was to adjust the timing for the interim and final analyses of the co-primary endpoint of overall survival, based upon overall survival data from a similar population of chemotherapy-naïve metastatic castration-resistant prostate cancer patients. The final overall survival analysis was modified to occur after a minimum of 765 death events, and the formal interim analysis at approximately 516 death events.<br><br>In addition, this amendment specified that independent central radiology review would continue until a minimum of 410 radiographic progression-free survival (rPFS) events occurred, and after that time scans only required local radiology review and confirmation. |
| 28 October 2013 | The main purpose of this amendment was to follow the Independent Data Monitoring Committee (IDMC) recommendation to halt the double-blind period of the study due to compelling clinical benefit of MDV3100 (enzalutamide) over placebo. The pre-planned interim analysis of overall survival and the final analysis of radiographic progression-free survival (rPFS) for this study showed statistically significant improvement in both co-primary endpoints, rPFS (hazard ratio = 0.19, $p < 0.0001$) and overall survival (hazard ratio = 0.70, $p < 0.0001$). This protocol amendment allowed all ongoing enzalutamide-treated patients and ongoing and previous placebo-treated patients the opportunity to receive open-label enzalutamide and continue in this protocol. |
| 29 April 2014 | The main purpose of this amendment was to remove the requirement for assessment of skeletal-related events during open-label treatment with enzalutamide because adequate information was obtained for this endpoint during the double-blind period. Additionally, the on-study requirement for 12-lead electrocardiograms (ECGs) was removed because no safety signals had been detected to date through ECG monitoring of more than 2500 patients during clinical development. |

Notes:

## Interruptions (globally)

Were there any global interruptions to the trial? No

## Limitations and caveats

None reported