# Clinical trial results:
# A Phase 3, Randomized, Double-Blind Study of Nivolumab or Placebo in Combination with Docetaxel, in Men with Metastatic Castration-resistant Prostate Cancer

## Summary

| | |
|---|---|
| EudraCT number | 2019-002030-36 |
| Trial protocol | GB ES DE FR BE CZ IT RO |
| Global end of trial date | 25 June 2024 |

### Results information

| | |
|---|---|
| Result version number | v1 (current) |
| This version publication date | 13 June 2025 |
| First version publication date | 13 June 2025 |

## Trial information

### Trial identification

| | |
|---|---|
| Sponsor protocol code | CA209-7DX |

### Additional study identifiers

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT04100018 |
| WHO universal trial number (UTN) | - |

Notes:

### Sponsors

| | |
|---|---|
| Sponsor organisation name | Bristol-Myers Squibb |
| Sponsor organisation address | Chaussée de la Hulpe 185, Brussels, Belgium, 1170 |
| Public contact | Global Submission Management, Clinical Trials, Bristol-Myers Squibb International Corporation, mg-gsm-ct@bms.com |
| Scientific contact | Global Submission Management, Clinical Trials, Bristol-Myers Squibb International Corporation, mg-gsm-ct@bms.com |

Notes:

### Paediatric regulatory details

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

Notes:

## Results analysis stage

| | |
|---|---|
| Analysis stage | Final |
| Date of interim/final analysis | 30 July 2024 |
| Is this the analysis of the primary completion data? | No |

| | |
|---|---|
| Global end of trial reached? | Yes |
| Global end of trial date | 25 June 2024 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

The purpose of this study is to assess the safety and effectiveness of nivolumab with docetaxel in men with advanced castration resistant prostate cancer who have progressed after second-generation hormonal manipulation.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Conference on Harmonization Good Clinical Practice Guidelines. All the local regulatory requirements pertinent to safety of trial participants were followed.

Background therapy: -

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 06 February 2020 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

## Population of trial subjects

### Subjects enrolled per country

| | |
|---|---|
| Country: Number of subjects enrolled | Canada: 5 |
| Country: Number of subjects enrolled | United States: 108 |
| Country: Number of subjects enrolled | Austria: 10 |
| Country: Number of subjects enrolled | Belgium: 20 |
| Country: Number of subjects enrolled | Czechia: 28 |
| Country: Number of subjects enrolled | France: 101 |
| Country: Number of subjects enrolled | Germany: 52 |
| Country: Number of subjects enrolled | Italy: 33 |
| Country: Number of subjects enrolled | Poland: 40 |
| Country: Number of subjects enrolled | Romania: 16 |
| Country: Number of subjects enrolled | Russian Federation: 24 |
| Country: Number of subjects enrolled | Spain: 77 |
| Country: Number of subjects enrolled | United Kingdom: 45 |
| Country: Number of subjects enrolled | China: 69 |
| Country: Number of subjects enrolled | Japan: 94 |
| Country: Number of subjects enrolled | Korea, Republic of: 39 |
| Country: Number of subjects enrolled | Taiwan: 18 |
| Country: Number of subjects enrolled | Hong Kong: 1 |
| Country: Number of subjects enrolled | Singapore: 12 |

| | |
|---|---|
| Country: Number of subjects enrolled | Argentina: 76 |
| Country: Number of subjects enrolled | Australia: 32 |
| Country: Number of subjects enrolled | Brazil: 70 |
| Country: Number of subjects enrolled | Chile: 10 |
| Country: Number of subjects enrolled | Israel: 17 |
| Country: Number of subjects enrolled | Mexico: 12 |
| Country: Number of subjects enrolled | New Zealand: 4 |
| Country: Number of subjects enrolled | Türkiye: 17 |
| Worldwide total number of subjects | 1030 |
| EEA total number of subjects | 377 |

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) | 268 |
| From 65 to 84 years | 745 |
| 85 years and over | 17 |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

1030 participants were randomized.

### Period 1

| | |
|---|---|
| Period 1 title | Pre-Treatment 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** | Nivolumab + Docetaxel + Prednisone |

Arm description:

Participants with metastatic castration resistant prostate cancer (mCRPC) who are chemotherapy-naïve for mCRPC and have received at least 1 but no more than 2 second-generation hormonal manipulations received Docetaxel 75 milligram per meter square (mg/m^2) intravenous (IV) once in a week (Q3W) + Prednisone 5 milligram (mg) orally (PO) twice a day (BID) + Nivolumab 360 mg IV Q3W for maximum 10 cycles, followed by Nivolumab 480 mg IV once in four weeks (Q4W) until disease progression or unacceptable toxicity or maximum of 2 years from the date of first dose or withdraw of consent.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Nivolumab |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

360 mg IV Q3W

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

Dosage and administration details:

75 mg/m² IV

| | |
|---|---|
| Investigational medicinal product name | Prednisone |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Chewable tablet |
| Routes of administration | Oral use |

Dosage and administration details:

5 mg PO BID

| | |
|---|---|
| **Arm title** | Placebo + Docetaxel + Prednisone |

Arm description:

Participants with metastatic castration resistant prostate cancer (mCRPC) who are chemotherapy-naïve for mCRPC and have received at least 1 but no more than 2 second-generation hormonal manipulations received Docetaxel 75 mg/m^2 IV Q3W + Prednisone 5 mg PO BID + Placebo IV Q3W for maximum 10 cycles, followed by Placebo IV Q4W until disease progression or unacceptable toxicity or maximum of 2

years from the date of first dose or withdraw of consent.

| | |
|---|---|
| Arm type | Active comparator |
| Investigational medicinal product name | Docetaxel |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

75 mg/m² IV

| | |
|---|---|
| Investigational medicinal product name | Prednisone |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Chewable tablet |
| Routes of administration | Oral use |

Dosage and administration details:

5 mg PO BID

| **Number of subjects in period 1** | Nivolumab + Docetaxel + Prednisone | Placebo + Docetaxel + Prednisone |
|---|---|---|
| Started | 514 | 516 |
| Completed | 510 | 510 |
| Not completed | 4 | 6 |
| Participant withdrew consent | 2 | - |
| Not Reported | - | 4 |
| Poor/Non-compliance | 1 | - |
| Subject no longer meets study criteria | 1 | 1 |
| Participant request to discontinue study treatment | - | 1 |

## Period 2

| | |
|---|---|
| Period 2 title | Treatment Period |
| Is this the baseline period? | No |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator |

## Arms

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

| **Arm title** | Nivolumab + Docetaxel + Prednisone |
|---|---|

Arm description:

Participants with metastatic castration resistant prostate cancer (mCRPC) who are chemotherapy-naïve for mCRPC and have received at least 1 but no more than 2 second-generation hormonal manipulations received Docetaxel 75 milligram per meter square (mg/m^2) intravenous (IV) once in a week (Q3W) + Prednisone 5 milligram (mg) orally (PO) twice a day (BID) + Nivolumab 360 mg IV Q3W for maximum 10 cycles, followed by Nivolumab 480 mg IV once in four weeks (Q4W) until disease progression or unacceptable toxicity or maximum of 2 years from the date of first dose or withdraw of consent.

| Arm type | Experimental |
|---|---|
| Investigational medicinal product name | Nivolumab |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

360 mg IV Q3W

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

Dosage and administration details:

75 mg/m² IV

| Investigational medicinal product name | Prednisone |
|---|---|
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Chewable tablet |
| Routes of administration | Oral use |

Dosage and administration details:

5 mg PO BID

| **Arm title** | Placebo + Docetaxel + Prednisone |
|---|---|

Arm description:

Participants with metastatic castration resistant prostate cancer (mCRPC) who are chemotherapy-naïve for mCRPC and have received at least 1 but no more than 2 second-generation hormonal manipulations received Docetaxel 75 mg/m^2 IV Q3W + Prednisone 5 mg PO BID + Placebo IV Q3W for maximum 10 cycles, followed by Placebo IV Q4W until disease progression or unacceptable toxicity or maximum of 2 years from the date of first dose or withdraw of consent.

| Arm type | Active comparator |
|---|---|
| Investigational medicinal product name | Prednisone |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Chewable tablet |
| Routes of administration | Oral use |

Dosage and administration details:

5 mg PO BID

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

Dosage and administration details:

75 mg/m² IV

| **Number of subjects in period 2** | Nivolumab + Docetaxel + Prednisone | Placebo + Docetaxel + Prednisone |
|---|---|---|
| Started | 510 | 510 |
| Completed | 19 | 11 |
| Not completed | 491 | 499 |
| Adverse event, serious fatal | 16 | 11 |
| Participant withdrew consent | 10 | 10 |
| Ongoing Treatment | 1 | - |
| Maximum clinical benefit | 3 | - |
| Other Reason | 26 | 37 |
| Poor/Non-compliance | 1 | - |
| Administrative reasons by sponsor | 16 | 30 |
| Completed treatment as per protocol | 1 | 2 |
| Disease Progression | 284 | 327 |
| Study drug toxicity | 67 | 28 |
| Adverse event, non-fatal | 14 | 6 |
| Adverse event unrelated to study drug | 13 | 12 |
| Lost to follow-up | 2 | 2 |
| Participant request to discontinue study treatment | 33 | 32 |
| Lack of efficacy | 4 | 2 |

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | Nivolumab + Docetaxel + Prednisone |
| Reporting group description: | |
| Participants with metastatic castration resistant prostate cancer (mCRPC) who are chemotherapy-naïve for mCRPC and have received at least 1 but no more than 2 second-generation hormonal manipulations received Docetaxel 75 milligram per meter square (mg/m^2) intravenous (IV) once in a week (Q3W) + Prednisone 5 milligram (mg) orally (PO) twice a day (BID) + Nivolumab 360 mg IV Q3W for maximum 10 cycles, followed by Nivolumab 480 mg IV once in four weeks (Q4W) until disease progression or unacceptable toxicity or maximum of 2 years from the date of first dose or withdraw of consent. | |
| Reporting group title | Placebo + Docetaxel + Prednisone |
| Reporting group description: | |
| Participants with metastatic castration resistant prostate cancer (mCRPC) who are chemotherapy-naïve for mCRPC and have received at least 1 but no more than 2 second-generation hormonal manipulations received Docetaxel 75 mg/m^2 IV Q3W + Prednisone 5 mg PO BID + Placebo IV Q3W for maximum 10 cycles, followed by Placebo IV Q4W until disease progression or unacceptable toxicity or maximum of 2 years from the date of first dose or withdraw of consent. | |

| Reporting group values | Nivolumab + Docetaxel + Prednisone | Placebo + Docetaxel + Prednisone | Total |
|---|---|---|---|
| Number of subjects | 514 | 516 | 1030 |
| Age categorical<br>Units: Subjects | | | |
| In utero | 0 | 0 | 0 |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | 0 |
| Newborns (0-27 days) | 0 | 0 | 0 |
| Infants and toddlers (28 days-23 months) | 0 | 0 | 0 |
| Children (2-11 years) | 0 | 0 | 0 |
| Adolescents (12-17 years) | 0 | 0 | 0 |
| Adults (18-64 years) | 139 | 129 | 268 |
| From 65-84 years | 370 | 375 | 745 |
| 85 years and over | 5 | 12 | 17 |
| Age Continuous<br>Units: years | | | |
| arithmetic mean | 68.9 | 69.6 | |
| standard deviation | ± 7.5 | ± 8.1 | - |
| Sex: Female, Male<br>Units: participants | | | |
| Female | 0 | 1 | 1 |
| Male | 514 | 515 | 1029 |
| Race/Ethnicity, Customized<br>Units: Subjects | | | |
| White | 333 | 329 | 662 |
| Black or African American | 20 | 15 | 35 |
| Asian | 35 | 45 | 80 |
| Native Hawaiian or other pacific islander | 1 | 0 | 1 |
| Chinese | 40 | 38 | 78 |
| Japanese | 33 | 45 | 78 |

| | | | |
|---|---|---|---|
| Asian other | 1 | 0 | 1 |
| Other | 30 | 27 | 57 |
| Not Reported | 19 | 16 | 35 |
| Asian Indian | 2 | 1 | 3 |

## End points

### End points reporting groups

| Reporting group title | Nivolumab + Docetaxel + Prednisone |
|---|---|

Reporting group description:

Participants with metastatic castration resistant prostate cancer (mCRPC) who are chemotherapy-naïve for mCRPC and have received at least 1 but no more than 2 second-generation hormonal manipulations received Docetaxel 75 milligram per meter square (mg/m^2) intravenous (IV) once in a week (Q3W) + Prednisone 5 milligram (mg) orally (PO) twice a day (BID) + Nivolumab 360 mg IV Q3W for maximum 10 cycles, followed by Nivolumab 480 mg IV once in four weeks (Q4W) until disease progression or unacceptable toxicity or maximum of 2 years from the date of first dose or withdraw of consent.

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

Reporting group description:

Participants with metastatic castration resistant prostate cancer (mCRPC) who are chemotherapy-naïve for mCRPC and have received at least 1 but no more than 2 second-generation hormonal manipulations received Docetaxel 75 mg/m^2 IV Q3W + Prednisone 5 mg PO BID + Placebo IV Q3W for maximum 10 cycles, followed by Placebo IV Q4W until disease progression or unacceptable toxicity or maximum of 2 years from the date of first dose or withdraw of consent.

| Reporting group title | Nivolumab + Docetaxel + Prednisone |
|---|---|

Reporting group description:

Participants with metastatic castration resistant prostate cancer (mCRPC) who are chemotherapy-naïve for mCRPC and have received at least 1 but no more than 2 second-generation hormonal manipulations received Docetaxel 75 milligram per meter square (mg/m^2) intravenous (IV) once in a week (Q3W) + Prednisone 5 milligram (mg) orally (PO) twice a day (BID) + Nivolumab 360 mg IV Q3W for maximum 10 cycles, followed by Nivolumab 480 mg IV once in four weeks (Q4W) until disease progression or unacceptable toxicity or maximum of 2 years from the date of first dose or withdraw of consent.

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

Reporting group description:

Participants with metastatic castration resistant prostate cancer (mCRPC) who are chemotherapy-naïve for mCRPC and have received at least 1 but no more than 2 second-generation hormonal manipulations received Docetaxel 75 mg/m^2 IV Q3W + Prednisone 5 mg PO BID + Placebo IV Q3W for maximum 10 cycles, followed by Placebo IV Q4W until disease progression or unacceptable toxicity or maximum of 2 years from the date of first dose or withdraw of consent.

### Primary: Radiographic Progressive Free Survival (rPFS) assessed by Blinded Independent Central Review (BICR) per Prostate Cancer Working Group 3 (PCWG3)

| End point title | Radiographic Progressive Free Survival (rPFS) assessed by Blinded Independent Central Review (BICR) per Prostate Cancer Working Group 3 (PCWG3) |
|---|---|

End point description:

rPFS for randomized participants is the time between randomization and the first date of documented progression or death due to any cause, whichever occurs first. The rPFS was censored at the last radiographic tumor assessment up to the start of subsequent cancer therapy for those without progression or death. It was also censored at the date of last radiographic tumor assessment prior to the missed tumor assessments for participants who had progressive disease (PD) or death immediately after more than one consecutive missed tumor assessments. Radiographic progression is defined as at least a 20% increase in the sum of diameters of target lesions, taking as reference the smallest sum on study (this includes the baseline sum if that is the smallest on study). In addition to the relative increase of 20%, the sum must also demonstrate an absolute increase of at least 5 millimeter (mm). The appearance of one or more new lesions is also considered progression.

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

End point timeframe:

from randomization to the first date of documented progression or death due to any cause, whichever occurs first (up to approximately 31 months)

| End point values | Nivolumab + Docetaxel + Prednisone | Placebo + Docetaxel + Prednisone | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 514 | 516 | | |
| Units: months | | | | |
| median (confidence interval 95%) | 9.43 (8.48 to 10.32) | 8.74 (8.38 to 9.99) | | |

## Statistical analyses

| Statistical analysis title | Statistical Analysis 1 |
|---|---|
| Comparison groups | Placebo + Docetaxel + Prednisone v Nivolumab + Docetaxel + Prednisone |
| Number of subjects included in analysis | 1030 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.5901 [1] |
| Method | Logrank |
| Parameter estimate | Cox proportional hazard |
| Point estimate | 0.96 |
| Confidence interval | |
| level | Other: 99 % |
| sides | 2-sided |
| lower limit | 0.77 |
| upper limit | 1.19 |

Notes:

[1] - Boundary for statistical significance p-value < 0.01

## Primary: Overall Survival (OS)

| End point title | Overall Survival (OS) |
|---|---|

End point description:

OS for all randomized participants is the time between randomization and the date of death from any cause. For participants who are alive, their survival time was censored at the last date that they were known to be alive. OS was censored for participants at the date of randomization if they had no follow-up.

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

End point timeframe:

From randomization to the date of death from any cause (Up to approximately 31 months)

| End point values | Nivolumab + Docetaxel + Prednisone | Placebo + Docetaxel + Prednisone | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 514 | 516 | | |
| Units: months | | | | |
| median (confidence interval 95%) | 18.73 (16.95 to 21.03) | 18.92 (17.31 to 22.01) | | |

### Statistical analyses

| Statistical analysis title | Statistical Analysis 1 |
|---|---|
| Comparison groups | Nivolumab + Docetaxel + Prednisone v Placebo + Docetaxel + Prednisone |
| Number of subjects included in analysis | 1030 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.3572 [2] |
| Method | Logrank |
| Parameter estimate | Cox proportional hazard |
| Point estimate | 1.09 |
| Confidence interval | |
| level | Other: 99.41 % |
| sides | 2-sided |
| lower limit | 0.84 |
| upper limit | 1.43 |

Notes:

[2] - Boundary for statistical significance p-value < 0.0059. Additional accuracy for p-value: 0.005866.

### Secondary: Time to Response (TTR) assessed by Blinded Independent Central Review (BICR) per Prostate Cancer Working Group (PCWG3)

| End point title | Time to Response (TTR) assessed by Blinded Independent Central Review (BICR) per Prostate Cancer Working Group (PCWG3) |
|---|---|

End point description:

Time to Response per PCWG3 (TTR-PCWG3) is the time from randomization to the date of the first documented CR or PR per PCWG3, as determined by BICR. Complete Response (CR) is defined as disappearance of all target lesions. Any pathological lymph nodes (whether target or non-target) must have reduction in short axis to < 10 mm. Partial Response (PR) is defined as at least a 30% decrease in the sum of diameters of target lesions, taking as reference the baseline sum diameters.

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

End point timeframe:

From randomization to the date of the first documented CR or PR (Up to approximately 52 months)

| End point values | Nivolumab + Docetaxel + Prednisone | Placebo + Docetaxel + Prednisone | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 59 | 48 | | |
| Units: months | | | | |
| median (full range (min-max)) | 2.17 (1.4 to 7.8) | 2.20 (1.7 to 8.2) | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Objective Response Rate (ORR) assessed by Blinded Independent Central Review (BICR) per Prostate Cancer Working Group (PCWG3)

| End point title | Objective Response Rate (ORR) assessed by Blinded Independent Central Review (BICR) per Prostate Cancer Working Group (PCWG3) |
|---|---|

End point description:

Objective Response Rate per PCWG3 (ORR-PCWG3) is the percentage of participants who have a confirmed complete or partial best overall response (BOR) per PCWG3 among randomized participants who have measurable disease at baseline. Complete Response (CR) is defined as disappearance of all target lesions. Any pathological lymph nodes (whether target or non-target) must have reduction in short axis to < 10 mm. Partial Response (PR) is defined as at least a 30% decrease in the sum of diameters of target lesions, taking as reference the baseline sum diameters. Baseline was defined as evaluations or events that occur before the date and time of the first dose of study treatment or evaluations on the same date and time of the first dose of study treatment were also considered as baseline evaluations.

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

End point timeframe:

From date of randomization to the date of objectively documented progression per PCWG3 or the date of subsequent systemic cancer therapy, whichever occurs first (Up to approximately 52 months)

| End point values | Nivolumab + Docetaxel + Prednisone | Placebo + Docetaxel + Prednisone | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 216 | 204 | | |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | 27.3 (21.5 to 33.8) | 23.5 (17.9 to 30.0) | | |

## Statistical analyses

| Statistical analysis title | Statistical Analysis 1 |
|---|---|
| Comparison groups | Nivolumab + Docetaxel + Prednisone v Placebo + Docetaxel + Prednisone |

| | |
|---|---|
| Number of subjects included in analysis | 420 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Adjusted Difference |
| Point estimate | 3.8 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -4.5 |
| upper limit | 12.1 |

## Secondary: Duration of Response assessed by Blinded Independent Central Review (BICR) per Prostate Cancer Working Group (PCWG3)

| | |
|---|---|
| End point title | Duration of Response assessed by Blinded Independent Central Review (BICR) per Prostate Cancer Working Group (PCWG3) |

End point description:

Duration of Response per PCWG3 (DOR-PCWG3) is time between the date of first response (CR/PR per PCWG3) to the date of first documented radiographic progression per PCWG3,as determined by BICR, or death due to any cause whichever occurs first. Complete Response (CR) is defined as disappearance of all target lesions. Any pathological lymph nodes (whether target or non-target) must have reduction in short axis to < 10 mm. Partial Response (PR) is defined as at least a 30% decrease in the sum of diameters of target lesions, taking as reference the baseline sum diameters. Radiographic progression was defined as at least a 20% increase in the sum of diameters of target lesions, taking as reference the smallest sum on study (this includes the baseline sum if that is the smallest on study). In addition to the relative increase of 20%, the sum must also demonstrate an absolute increase of at least 5 millimeter (mm). The appearance of one or more new lesions is also considered progression.

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

End point timeframe:

From randomization date to the date of first documented radiographic progression or death due to any cause whichever occurs first (Up to approximately 52 months)

| **End point values** | Nivolumab + Docetaxel + Prednisone | Placebo + Docetaxel + Prednisone | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 59 | 48 | | |
| Units: months | | | | |
| median (confidence interval 95%) | 8.31 (6.18 to 10.15) | 8.11 (6.34 to 8.74) | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Prostate-specific antigen (PSA) Response Rate (PSA-RR)

| | |
|---|---|
| End point title | Prostate-specific antigen (PSA) Response Rate (PSA-RR) |

End point description:

PSA Response Rate (PSA-RR) is the percentage of randomized participants with a 50% or greater

decrease in PSA from baseline to the lowest post-baseline PSA result. A second consecutive value obtained 3 or more weeks later is required to confirm the PSA response. Baseline was defined as valuations or events that occur before the date and time of the first dose of study treatment or evaluations on the same date and time of the first dose of study treatment were also considered as baseline evaluations.

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

End point timeframe:

Up to approximately 52 months

| **End point values** | Nivolumab + Docetaxel + Prednisone | Placebo + Docetaxel + Prednisone | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 498 | 503 | | |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | 42.4 (38.0 to 46.8) | 41.6 (37.2 to 46.0) | | |

**Statistical analyses**

| **Statistical analysis title** | Statistical Analysis 1 |
|---|---|
| Comparison groups | Nivolumab + Docetaxel + Prednisone v Placebo + Docetaxel + Prednisone |
| Number of subjects included in analysis | 1001 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Percentage Difference |
| Point estimate | 0.9 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -5.2 |
| upper limit | 7 |

## Secondary: Time to PSA Progression (TTP-PSA)

| End point title | Time to PSA Progression (TTP-PSA) |
|---|---|

End point description:

Time to PSA Progression (TTP-PSA) is the time between randomization to the date of PSA progression per PCWG3 in randomized participants. PSA Progression: For participants with an initial PSA decline from baseline, the date of PSA progression is the date that an increase of 25% or more and an absolute increase of 2 ng/mL or more from the nadir are documented and confirmed by a second consecutive PSA value at least 3 weeks later. For participants with no PSA decline from baseline, the date of PSA progression is date that an increase of 25% or more and an absolute increase of 2 ng/mL or more from baseline are documented at or beyond Week 13. Baseline was defined as valuations or events that occur before the date and time of the first dose of study treatment or evaluations on the same date and time of the first dose of study treatment were also considered as baseline evaluations. Censored at date of last PSA evaluation on/prior to start of subsequent cancer therapy.

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

End point timeframe:

from randomization to the date of PSA Progression (Up to approximately 31 months)

| **End point values** | Nivolumab + Docetaxel + Prednisone | Placebo + Docetaxel + Prednisone | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 514 | 516 | | |
| Units: months | | | | |
| median (confidence interval 95%) | 6.28 (5.82 to 6.97) | 6.21 (5.65 to 6.77) | | |

**Statistical analyses**

| **Statistical analysis title** | Statistical Analysis 1 |
|---|---|
| Comparison groups | Nivolumab + Docetaxel + Prednisone v Placebo + Docetaxel + Prednisone |
| Number of subjects included in analysis | 1030 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Cox proportional hazard |
| Point estimate | 1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.86 |
| upper limit | 1.16 |

**Secondary: Number of Participants with Adverse Events**

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

End point description:

An Adverse Event (AE) is defined as any new untoward medical occurrence or worsening of a preexisting medical condition in a clinical investigation participant administered study treatment and that does not necessarily have a causal relationship with this treatment. An AE can therefore be any unfavorable and unintended sign (such as an abnormal laboratory finding), symptom, or disease temporally associated with the use of study treatment, whether or not considered related to the study treatment.

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

End point timeframe:

From first dose and 30 days after last dose of study therapy (Up to approximately 25 months)

| End point values | Nivolumab + Docetaxel + Prednisone | Placebo + Docetaxel + Prednisone | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 510 | 510 | | |
| Units: participants | 501 | 503 | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Participants with Endocrine Immune-Mediated Adverse Events

| End point title | Number of Participants with Endocrine Immune-Mediated Adverse Events |
|---|---|

End point description:

Immune-mediated adverse events are AEs consistent with an immune-mediated mechanism or immune-mediated component for which non-inflammatory etiologies (eg, infection or tumor progression) have been ruled out. IMAEs can include events with an alternate etiology which were exacerbated by the induction of autoimmunity. An Adverse Event (AE) is defined as any new untoward medical occurrence or worsening of a preexisting medical condition in a clinical investigation participant administered study treatment and that does not necessarily have a causal relationship with this treatment. An AE can therefore be any unfavorable and unintended sign (such as an abnormal laboratory finding), symptom, or disease temporally associated with the use of study treatment, whether or not considered related to the study treatment.

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

End point timeframe:

From first dose and 100 days after last dose of study therapy (Up to approximately 13 months)

| End point values | Nivolumab + Docetaxel + Prednisone | Placebo + Docetaxel + Prednisone | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 510 | 510 | | |
| Units: participants | | | | |
| Adrenal insufficiency | 7 | 4 | | |
| Hypothyroidism | 27 | 11 | | |
| Thyroiditis | 1 | 0 | | |
| Diabetes mellitus | 1 | 2 | | |
| Diabetic ketoacidosis | 1 | 0 | | |
| Type 1 diabetes mellitus | 1 | 0 | | |
| Hyperthyroidism | 20 | 11 | | |
| Immune-mediated hypophysitis | 1 | 0 | | |
| Hypopituitarism | 0 | 1 | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Participants with Serious Adverse Events

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

End point description:

Serious Adverse Event (SAE) is defined as any untoward medical occurrence that, at any dose results in death or Is life-threatening or requires inpatient hospitalization or causes prolongation of existing hospitalization or results in persistent or significant disability/incapacity or is a congenital anomaly/birth defect.

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

End point timeframe:

From first dose and 30 days after last dose of study therapy (Up to approximately 25 months)

| **End point values** | Nivolumab + Docetaxel + Prednisone | Placebo + Docetaxel + Prednisone | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 510 | 510 | | |
| Units: participants | 223 | 192 | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Participants with Adverse Events Leading to Discontinuation

| End point title | Number of Participants with Adverse Events Leading to Discontinuation |
|---|---|

End point description:

An Adverse Event (AE) is defined as any new untoward medical occurrence or worsening of a preexisting medical condition in a clinical investigation participant administered study treatment and that does not necessarily have a causal relationship with this treatment. An AE can therefore be any unfavorable and unintended sign (such as an abnormal laboratory finding), symptom, or disease temporally associated with the use of study treatment, whether or not considered related to the study treatment.

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

End point timeframe:

From first dose and 30 days after last dose of study therapy (Up to approximately 25 months)

| **End point values** | Nivolumab + Docetaxel + Prednisone | Placebo + Docetaxel + Prednisone | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 510 | 510 | | |
| Units: participants | 148 | 101 | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Participants with Non-Endocrine Immune-Mediated Adverse Events

| End point title | Number of Participants with Non-Endocrine Immune-Mediated Adverse Events |
|---|---|

End point description:

Immune-mediated adverse events are AEs consistent with an immune-mediated mechanism or immune-mediated component for which non-inflammatory etiologies (eg, infection or tumor progression) have been ruled out. IMAEs can include events with an alternate etiology which were exacerbated by the induction of autoimmunity. An Adverse Event (AE) is defined as any new untoward medical occurrence or worsening of a preexisting medical condition in a clinical investigation participant administered study treatment and that does not necessarily have a causal relationship with this treatment. An AE can therefore be any unfavorable and unintended sign (such as an abnormal laboratory finding), symptom, or disease temporally associated with the use of study treatment, whether or not considered related to the study treatment.

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

End point timeframe:

From first dose and 100 days after last dose of study therapy (Up to approximately 13 months)

| End point values | Nivolumab + Docetaxel + Prednisone | Placebo + Docetaxel + Prednisone | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 510 | 510 | | |
| Units: participants | | | | |
| Pneumonitis | 15 | 2 | | |
| Interstitial lung disease | 5 | 1 | | |
| Immune-mediated lung disease | 1 | 0 | | |
| Diarrhoea | 8 | 2 | | |
| Colitis | 4 | 0 | | |
| Enterocolitis | 1 | 0 | | |
| Alanine aminotransferase increased | 5 | 0 | | |
| Aspartate aminotransferase increased | 3 | 0 | | |
| Hypertransaminasaemia | 3 | 0 | | |
| Autoimmune hepatitis | 2 | 0 | | |
| Immune-mediated hepatitis | 2 | 0 | | |
| Blood bilirubin increased | 1 | 0 | | |
| Cholangitis | 1 | 0 | | |
| Blood creatinine increased | 1 | 0 | | |
| Acute kidney injury | 0 | 1 | | |
| Immune-mediated nephritis | 0 | 1 | | |
| Rash | 14 | 7 | | |
| Rash maculo-papular | 3 | 0 | | |
| Rash pustular | 2 | 0 | | |
| Dermatitis | 1 | 1 | | |
| Dermatitis acneiform | 1 | 0 | | |
| Drug eruption | 1 | 0 | | |
| Pemphigoid | 1 | 0 | | |
| Erythema multiforme | 0 | 1 | | |

| | | | | |
|---|---|---|---|---|
| Immune-mediated dermatitis | 0 | 1 | | |
| Rash macular | 0 | 1 | | |
| Infusion related reaction | 3 | 3 | | |
| Hypersensitivity | 0 | 1 | | |
| Infusion related hypersensitivity reaction | 0 | 1 | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Participants with Select Adverse Events

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

End point description:

An Adverse Event (AE) is defined as any new untoward medical occurrence or worsening of a preexisting medical condition in a clinical investigation participant administered study treatment and that does not necessarily have a causal relationship with this treatment. An AE can therefore be any unfavorable and unintended sign (such as an abnormal laboratory finding), symptom, or disease temporally associated with the use of study treatment, whether or not considered related to the study treatment.

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

End point timeframe:

From first dose and 30 days after last dose of study therapy (Up to approximately 25 months)

| End point values | Nivolumab + Docetaxel + Prednisone | Placebo + Docetaxel + Prednisone | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 510 | 510 | | |
| Units: participants | | | | |
| Diarrhoea | 176 | 159 | | |
| Colitis | 7 | 2 | | |
| Enterocolitis | 2 | 1 | | |
| Frequent bowel movements | 0 | 1 | | |
| Alanine aminotransferase increased | 36 | 14 | | |
| Aspartate aminotransferase increased | 26 | 15 | | |
| Blood alkaline phosphatase increased | 23 | 22 | | |
| Blood bilirubin increased | 8 | 4 | | |
| Gamma-glutamyltransferase increased | 5 | 3 | | |
| Hepatic cytolysis | 4 | 1 | | |
| Transaminases increased | 4 | 1 | | |
| Autoimmune hepatitis | 2 | 0 | | |
| Cholangitis | 2 | 0 | | |
| Hyperbilirubinaemia | 2 | 2 | | |
| Hypertransaminasaemia | 2 | 0 | | |
| Hepatic enzyme increased | 1 | 2 | | |
| Hepatitis | 1 | 0 | | |
| Immune-mediated hepatitis | 1 | 0 | | |
| Liver injury | 1 | 0 | | |

| | | | | |
|---|---|---|---|---|
| Liver disorder | 0 | 1 | | |
| Pneumonitis | 26 | 6 | | |
| Interstitial lung disease | 7 | 4 | | |
| Acute respiratory failure | 1 | 0 | | |
| Immune-mediated lung disease | 1 | 0 | | |
| Lung infiltration | 1 | 0 | | |
| Idiopathic interstitial pneumonia | 0 | 1 | | |
| Blood creatinine increased | 22 | 7 | | |
| Acute kidney injury | 7 | 9 | | |
| Renal failure | 3 | 5 | | |
| Blood urea increased | 2 | 2 | | |
| Immune-mediated nephritis | 0 | 1 | | |
| Rash | 51 | 34 | | |
| Pruritus | 47 | 20 | | |
| Eczema | 10 | 3 | | |
| Rash maculo-papular | 11 | 6 | | |
| Dermatitis | 6 | 4 | | |
| Palmar-plantar erythrodysaesthesia syndrome | 5 | 22 | | |
| Urticaria | 5 | 3 | | |
| Erythema | 4 | 11 | | |
| Psoriasis | 4 | 3 | | |
| Skin exfoliation | 4 | 2 | | |
| Dermatitis acneiform | 3 | 1 | | |
| Rash macular | 3 | 2 | | |
| Dermatitis allergic | 2 | 0 | | |
| Rash erythematous | 2 | 2 | | |
| Rash pustular | 3 | 0 | | |
| Vitiligo | 2 | 1 | | |
| Blister | 1 | 0 | | |
| Dermatitis atopic | 1 | 2 | | |
| Dermatitis exfoliative | 1 | 0 | | |
| Drug eruption | 1 | 0 | | |
| Erythema multiforme | 1 | 1 | | |
| Exfoliative rash | 1 | 0 | | |
| Pemphigoid | 1 | 0 | | |
| Photosensitivity reaction | 1 | 0 | | |
| Rash papular | 1 | 1 | | |
| Rash pruritic | 1 | 0 | | |
| Immune-mediated dermatitis | 0 | 1 | | |
| Infusion related reaction | 22 | 27 | | |
| Hypersensitivity | 6 | 4 | | |
| Anaphylactic reaction | 1 | 0 | | |
| Anaphylactic shock | 1 | 0 | | |
| Bronchospasm | 0 | 1 | | |
| Infusion related hypersensitivity reaction | 0 | 3 | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Participants who Died

| End point title | Number of Participants who Died |
|---|---|

End point description:

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

End point timeframe:

Up to approximately 52 months

| End point values | Nivolumab + Docetaxel + Prednisone | Placebo + Docetaxel + Prednisone | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 510 | 510 | | |
| Units: participants | 258 | 227 | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Participants with Worst Common Terminology Criteria (CTC) Grade Laboratory Test Grade Change from Baseline

| End point title | Number of Participants with Worst Common Terminology Criteria (CTC) Grade Laboratory Test Grade Change from Baseline |
|---|---|

End point description:

The severity of laboratory test results were graded based upon the participants symptoms according to the Common Terminology Criteria for Adverse Events (CTCAE, Version 5.0); Hematology parameters were evaluated for severity according to the following scale: Grade 0 is defined as absence of an AE or within normal limits; Grade 1 = Mild - transient or mild discomfort; no medical intervention required; Grade 2 = Moderate - mild to moderate limitation in activity; Grade 3 = Severe; Grade 4 = Life threatening. Number of participants with worst grade change results to Grade 3 or Grade 4 laboratory test results is presented. E.g., the row title HEMOGLOBIN Grade 0 to Grade 3, Grade 0 is baseline and Grade 3 is post baseline.

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

End point timeframe:

From first dose and 30 days after last dose of study therapy (Up to approximately 25 months)

| End point values | Nivolumab + Docetaxel + Prednisone | Placebo + Docetaxel + Prednisone | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 510 | 510 | | |
| Units: Participants | | | | |
| HEMOGLOBIN Grade 0 to Grade 3 | 5 | 3 | | |
| HEMOGLOBIN Grade 0 to Grade 4 | 99999 | 99999 | | |

| | | | | |
|---|---|---|---|---|
| HEMOGLOBIN Grade 1 to Grade 3 | 20 | 16 | | |
| HEMOGLOBIN Grade 1 to Grade 4 | 99999 | 99999 | | |
| HEMOGLOBIN Grade 2 to Grade 3 | 11 | 11 | | |
| HEMOGLOBIN Grade 2 to Grade 4 | 99999 | 99999 | | |
| HEMOGLOBIN Grade 3 to Grade 3 | 0 | 0 | | |
| HEMOGLOBIN Grade 3 to Grade 4 | 99999 | 99999 | | |
| PLATELET COUNT Grade 0 to Grade 3 | 2 | 3 | | |
| PLATELET COUNT Grade 0 to Grade 4 | 0 | 1 | | |
| PLATELET COUNT Grade 1 to Grade 3 | 2 | 1 | | |
| PLATELET COUNT Grade 1 to Grade 4 | 1 | 1 | | |
| PLATELET COUNT Grade 2 to Grade 3 | 0 | 0 | | |
| PLATELET COUNT Grade 2 to Grade 4 | 0 | 0 | | |
| PLATELET COUNT Grade 3 to Grade 3 | 0 | 0 | | |
| PLATELET COUNT Grade 3 to Grade 4 | 0 | 0 | | |
| PLATELET COUNT Grade 4 to Grade 3 | 0 | 0 | | |
| PLATELET COUNT Grade 4 to Grade 4 | 0 | 0 | | |
| LEUKOCYTES Grade 0 to Grade 3 | 30 | 28 | | |
| LEUKOCYTES Grade 0 to Grade 4 | 11 | 13 | | |
| LEUKOCYTES Grade 1 to Grade 3 | 5 | 3 | | |
| LEUKOCYTES Grade 1 to Grade 4 | 1 | 1 | | |
| LEUKOCYTES Grade 2 to Grade 3 | 0 | 1 | | |
| LEUKOCYTES Grade 2 to Grade 4 | 0 | 0 | | |
| LEUKOCYTES Grade 3 to Grade 3 | 0 | 0 | | |
| LEUKOCYTES Grade 3 to Grade 4 | 0 | 0 | | |
| LEUKOCYTES Grade 4 to Grade 3 | 0 | 0 | | |
| LEUKOCYTES Grade 4 to Grade 4 | 0 | 0 | | |
| LYMPHOCYTES Grade 0 to Grade 3 | 22 | 17 | | |
| LYMPHOCYTES Grade 0 to Grade 4 | 1 | 1 | | |
| LYMPHOCYTES Grade 1 to Grade 3 | 24 | 22 | | |
| LYMPHOCYTES Grade 1 to Grade 4 | 3 | 1 | | |
| LYMPHOCYTES Grade 2 to Grade 3 | 19 | 30 | | |
| LYMPHOCYTES Grade 2 to Grade 4 | 2 | 2 | | |
| LYMPHOCYTES Grade 3 to Grade 3 | 10 | 19 | | |
| LYMPHOCYTES Grade 3 to Grade 4 | 2 | 4 | | |
| LYMPHOCYTES Grade 4 to Grade 3 | 0 | 0 | | |
| LYMPHOCYTES Grade 4 to Grade 4 | 0 | 0 | | |
| ANC Grade 0 to Grade 3 | 18 | 16 | | |
| ANC Grade 0 to Grade 4 | 44 | 39 | | |
| ANC Grade 1 to Grade 3 | 0 | 0 | | |
| ANC Grade 1 to Grade 4 | 0 | 1 | | |
| ANC Grade 2 to Grade 3 | 0 | 1 | | |
| ANC Grade 2 to Grade 4 | 0 | 1 | | |
| ANC Grade 3 to Grade 3 | 0 | 0 | | |
| ANC Grade 3 to Grade 4 | 0 | 0 | | |
| ANC Grade 4 to Grade 3 | 0 | 0 | | |
| ANC Grade 4 to Grade 4 | 0 | 0 | | |
| ALP Grade 0 to Grade 3 | 5 | 1 | | |
| ALP Grade 0 to Grade 4 | 0 | 0 | | |
| ALP Grade 1 to Grade 3 | 1 | 1 | | |
| ALP Grade 1 to Grade 4 | 0 | 0 | | |
| ALP Grade 2 to Grade 3 | 0 | 0 | | |
| ALP Grade 2 to Grade 4 | 0 | 0 | | |

| | | | | |
|---|---|---|---|---|
| ALP Grade 3 to Grade 4 | 0 | 0 | | |
| ALP Grade 4 to Grade 3 | 0 | 0 | | |
| ALP Grade 4 to Grade 4 | 0 | 0 | | |
| AMT Grade 0 to Grade 3 | 6 | 0 | | |
| AMT Grade 0 to Grade 4 | 1 | 0 | | |
| AMT Grade 1 to Grade 3 | 1 | 2 | | |
| AMT Grade 1 to Grade 4 | 1 | 1 | | |
| AMT Grade 2 to Grade 3 | 0 | 0 | | |
| AMT Grade 2 to Grade 4 | 0 | 0 | | |
| AMT Grade 3 to Grade 3 | 0 | 0 | | |
| AMT Grade 3 to Grade 4 | 0 | 0 | | |
| AMT Grade 4 to Grade 3 | 0 | 0 | | |
| AMT Grade 4 to Grade 4 | 0 | 0 | | |
| ALT Grade 0 to Grade 3 | 7 | 2 | | |
| ALT Grade 0 to Grade 4 | 3 | 0 | | |
| ALT Grade 1 to Grade 3 | 0 | 0 | | |
| ALT Grade 1 to Grade 4 | 0 | 0 | | |
| ALT Grade 2 to Grade 3 | 0 | 0 | | |
| ALT Grade 3 to Grade 3 | 0 | 0 | | |
| ALT Grade 4 to Grade 3 | 0 | 0 | | |
| ALT Grade 4 to Grade 4 | 0 | 0 | | |
| BILIRUBIN Grade 0 to Grade 3 | 2 | 1 | | |
| BILIRUBIN Grade 0 to Grade 4 | 1 | 0 | | |
| BILIRUBIN Grade 1 to Grade 3 | 0 | 0 | | |
| BILIRUBIN Grade 1 to Grade 4 | 0 | 0 | | |
| BILIRUBIN Grade 2 to Grade 3 | 0 | 0 | | |
| BILIRUBIN Grade 2 to Grade 4 | 0 | 0 | | |
| BILIRUBIN Grade 3 to Grade 3 | 0 | 0 | | |
| BILIRUBIN Grade 3 to Grade 4 | 0 | 0 | | |
| BILIRUBIN Grade 4 to Grade 3 | 0 | 0 | | |
| BILIRUBIN Grade 4 to Grade 4 | 0 | 0 | | |
| CREATININE Grade 0 to Grade 3 | 4 | 4 | | |
| CREATININE Grade 0 to Grade 4 | 0 | 0 | | |
| CREATININE Grade 1 to Grade 3 | 1 | 0 | | |
| CREATININE Grade 1 to Grade 4 | 1 | 0 | | |
| CREATININE Grade 2 to Grade 3 | 0 | 1 | | |
| CREATININE Grade 2 to Grade 4 | 1 | 0 | | |
| CREATININE Grade 3 to Grade 3 | 0 | 0 | | |
| CREATININE Grade 3 to Grade 4 | 0 | 0 | | |
| CREATININE Grade 4 to Grade 3 | 0 | 0 | | |
| CREATININE Grade 4 to Grade 4 | 0 | 0 | | |
| HYPERNATREMIA Grade 0 to Grade 3 | 0 | 0 | | |
| HYPERNATREMIA Grade 0 to Grade 4 | 0 | 0 | | |
| HYPERNATREMIA Grade 1 to Grade 3 | 0 | 0 | | |
| HYPERNATREMIA Grade 1 to Grade 4 | 0 | 0 | | |
| HYPERNATREMIA Grade 2 to Grade 3 | 0 | 0 | | |
| HYPERNATREMIA Grade 2 to Grade 4 | 0 | 0 | | |
| HYPERNATREMIA Grade 3 to Grade 3 | 0 | 0 | | |
| HYPERNATREMIA Grade 3 to Grade 4 | 0 | 0 | | |
| HYPERNATREMIA Grade 4 to Grade 3 | 0 | 0 | | |
| HYPERNATREMIA Grade 4 to Grade 4 | 0 | 0 | | |
| HYPONATREMIA Grade 0 to Grade 3 | 5 | 4 | | |

| | | | | |
|---|---|---|---|---|
| HYPONATREMIA Grade 0 to Grade 4 | 0 | 1 | | |
| HYPONATREMIA Grade 1 to Grade 3 | 0 | 0 | | |
| HYPONATREMIA Grade 1 to Grade 4 | 0 | 1 | | |
| HYPONATREMIA Grade 2 to Grade 3 | 0 | 0 | | |
| HYPONATREMIA Grade 2 to Grade 4 | 0 | 0 | | |
| HYPONATREMIA Grade 3 to Grade 3 | 0 | 0 | | |
| HYPONATREMIA Grade 3 to Grade 4 | 0 | 0 | | |
| HYPONATREMIA Grade 4 to Grade 3 | 0 | 0 | | |
| HYPONATREMIA Grade 4 to Grade 4 | 0 | 0 | | |
| HYPERKALEMIA Grade 0 to Grade 3 | 8 | 1 | | |
| HYPERKALEMIA Grade 0 to Grade 4 | 2 | 1 | | |
| HYPERKALEMIA Grade 1 to Grade 3 | 2 | 0 | | |
| HYPERKALEMIA Grade 1 to Grade 4 | 0 | 1 | | |
| HYPERKALEMIA Grade 2 to Grade 3 | 1 | 0 | | |
| HYPERKALEMIA Grade 2 to Grade 4 | 0 | 0 | | |
| HYPERKALEMIA Grade 3 to Grade 3 | 0 | 0 | | |
| HYPERKALEMIA Grade 3 to Grade 4 | 0 | 0 | | |
| HYPERKALEMIA Grade 4 to Grade 3 | 0 | 0 | | |
| HYPERKALEMIA Grade 4 to Grade 4 | 0 | 0 | | |
| HYPOKALEMIA Grade 0 to Grade 3 | 7 | 8 | | |
| HYPOKALEMIA Grade 0 to Grade 4 | 1 | 0 | | |
| HYPOKALEMIA Grade 1 to Grade 3 | 3 | 1 | | |
| HYPOKALEMIA Grade 1 to Grade 4 | 0 | 0 | | |
| HYPOKALEMIA Grade 2 to Grade 3 | 0 | 0 | | |
| HYPOKALEMIA Grade 2 to Grade 4 | 0 | 0 | | |
| HYPOKALEMIA Grade 3 to Grade 3 | 0 | 0 | | |
| HYPOKALEMIA Grade 3 to Grade 4 | 0 | 0 | | |
| HYPOKALEMIA Grade 4 to Grade 3 | 0 | 0 | | |
| HYPOKALEMIA Grade 4 to Grade 4 | 0 | 0 | | |
| HYPERCALCEMIA Grade 0 to Grade 3 | 0 | 0 | | |
| HYPERCALCEMIA Grade 0 to Grade 4 | 0 | 0 | | |
| HYPERCALCEMIA Grade 1 to Grade 3 | 0 | 0 | | |
| HYPERCALCEMIA Grade 1 to Grade 4 | 1 | 0 | | |
| HYPERCALCEMIA Grade 2 to Grade 3 | 0 | 0 | | |
| HYPERCALCEMIA Grade 2 to Grade 4 | 0 | 0 | | |
| HYPERCALCEMIA Grade 3 to Grade 3 | 0 | 0 | | |
| HYPERCALCEMIA Grade 3 to Grade 4 | 0 | 0 | | |
| HYPERCALCEMIA Grade 4 to Grade 3 | 0 | 0 | | |
| HYPERCALCEMIA Grade 4 to Grade 4 | 0 | 0 | | |
| HYPOCALCEMIA Grade 0 to Grade 3 | 6 | 4 | | |
| HYPOCALCEMIA Grade 0 to Grade 4 | 1 | 0 | | |
| HYPOCALCEMIA Grade 1 to Grade 3 | 1 | 2 | | |
| HYPOCALCEMIA Grade 1 to Grade 4 | 0 | 0 | | |
| HYPOCALCEMIA Grade 2 to Grade 3 | 3 | 0 | | |
| HYPOCALCEMIA Grade 2 to Grade 4 | 3 | 0 | | |
| HYPOCALCEMIA Grade 3 to Grade 3 | 0 | 0 | | |
| HYPOCALCEMIA Grade 3 to Grade 4 | 0 | 0 | | |
| HYPOCALCEMIA Grade 4 to Grade 3 | 0 | 0 | | |
| HYPOCALCEMIA Grade 4 to Grade 4 | 0 | 0 | | |
| HYPERMAGNESEMIA Grade 0 to Grade 3 | 4 | 3 | | |
| HYPERMAGNESEMIA Grade 0 to Grade 4 | 0 | 0 | | |
| HYPERMAGNESEMIA Grade 1 to Grade 3 | 1 | 0 | | |

| | | | | |
|---|---|---|---|---|
| HYPERMAGNESEMIA Grade 1 to Grade 4 | 0 | 0 | | |
| HYPERMAGNESEMIA Grade 2 to Grade 3 | 0 | 0 | | |
| HYPERMAGNESEMIA Grade 2 to Grade 4 | 0 | 0 | | |
| HYPERMAGNESEMIA Grade 3 to Grade 3 | 1 | 0 | | |
| HYPERMAGNESEMIA Grade 3 to Grade 4 | 0 | 0 | | |
| HYPERMAGNESEMIA Grade 4 to Grade 3 | 0 | 0 | | |
| HYPERMAGNESEMIA Grade 4 to Grade 4 | 0 | 0 | | |
| HYPOMAGNESEMIA Grade 0 to Grade 3 | 0 | 0 | | |
| HYPOMAGNESEMIA Grade 0 to Grade 4 | 0 | 0 | | |
| HYPOMAGNESEMIA Grade 1 to Grade 3 | 0 | 0 | | |
| HYPOMAGNESEMIA Grade 1 to Grade 4 | 0 | 0 | | |
| HYPOMAGNESEMIA Grade 2 to Grade 3 | 0 | 0 | | |
| HYPOMAGNESEMIA Grade 2 to Grade 4 | 0 | 0 | | |
| HYPOMAGNESEMIA Grade 3 to Grade 3 | 0 | 0 | | |
| HYPOMAGNESEMIA Grade 3 to Grade 4 | 0 | 0 | | |
| HYPOMAGNESEMIA Grade 4 to Grade 3 | 0 | 0 | | |
| HYPOMAGNESEMIA Grade 4 to Grade 4 | 0 | 0 | | |
| HYPOGLYCEMIA Grade 0 to Grade 3 | 1 | 1 | | |
| HYPOGLYCEMIA Grade 0 to Grade 4 | 1 | 0 | | |
| HYPOGLYCEMIA Grade 1 to Grade 3 | 0 | 0 | | |
| HYPOGLYCEMIA Grade 1 to Grade 4 | 0 | 0 | | |
| HYPOGLYCEMIA Grade 2 to Grade 3 | 0 | 0 | | |
| HYPOGLYCEMIA Grade 2 to Grade 4 | 0 | 0 | | |
| HYPOGLYCEMIA Grade 3 to Grade 3 | 0 | 0 | | |
| HYPOGLYCEMIA Grade 3 to Grade 4 | 0 | 0 | | |
| HYPOGLYCEMIA Grade 4 to Grade 3 | 0 | 0 | | |
| HYPOGLYCEMIA Grade 4 to Grade 4 | 0 | 0 | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Participants with Laboratory Abnormalities in Specific Thyroid Tests

| End point title | Number of Participants with Laboratory Abnormalities in Specific Thyroid Tests |
|---|---|

End point description:

Blood samples were collected for conducting specific thyroid test. Baseline is defined as evaluations or events that occur before the date and time of the first dose of study treatment. Baseline was defined as evaluations or events that occur before the date and time of the first dose of study treatment or evaluations on the same date and time of the first dose of study treatment were also considered as baseline evaluations.

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

End point timeframe:

From first dose and 30 days after last dose of study therapy (Up to approximately 11 months)

| End point values | Nivolumab + Docetaxel + Prednisone | Placebo + Docetaxel + Prednisone | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 499 | 502 | | |
| Units: participants | | | | |
| TSH > (Upper Limit of Normal) ULN | 94 | 77 | | |
| TSH > ULN with TSH <= ULN | 79 | 54 | | |
| TSH > ULN with at Least One FT3/FT4 < LLN | 39 | 20 | | |
| TSH > ULN With All Other FT3/FT4 >= LLN | 65 | 52 | | |
| TSH > ULN with FT3/FT4 Test Missing | 22 | 23 | | |
| TSH < Lower Limit of Normal (LLN) | 155 | 124 | | |
| TSH < LLN with TSH >= LLN at Baseline | 126 | 98 | | |
| TSH < LLN with at Least One FT3/FT4 > ULN | 33 | 14 | | |
| TSH < LLN with all other FT3/FT4 <= ULN | 116 | 106 | | |
| TSH < LLN with FT3/FT4 Test Missing | 45 | 24 | | |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Time to Pain Progression as assessed by Brief Pain Inventory-Short Form (BPI-SF)

| End point title | Time to Pain Progression as assessed by Brief Pain Inventory-Short Form (BPI-SF) |
|---|---|

End point description:

The BPI-SF is an instrument to assess pain and includes severity and interference scores. BPI-SF is an 11-item self-report questionnaire designed to assess severity and impact of pain on daily function. Participants rate severity of pain at its “worst,” “least,” and “average” in last 24 hours using an 11-point numerical rating scale with anchors of “no pain” and “pain as bad. The participant’s assessment of pain with BPI-SF Item number 3 (pain symptoms at their worst over the last 24 hours) form basis for analysis. Time to pain progression is time between date of randomization and date of first increase in worst pain intensity. Pain progression occurred if an increase in worst pain intensity of >= 2 points is observed from baseline and maintained over 2 consecutive time periods. Baseline was evaluations or events that occur before date and time of first dose of study treatment or evaluations on same date and time of first dose of study treatment were also considered as baseline.

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

End point timeframe:

From randomization to 1st pain symptoms at their worst over the last 24 hours (Up to approximately 31 months

| End point values | Nivolumab + Docetaxel + Prednisone | Placebo + Docetaxel + Prednisone | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 514 | 516 | | |
| Units: months | | | | |
| median (confidence interval 95%) | 11.53 (10.28 | 12.42 (11.07 | | |

| | |
|---|---|
| to 13.57) | to 13.63) |

## Statistical analyses

No statistical analyses for this end point

## Adverse events information

Timeframe for reporting adverse events:

All cause mortality was collected from randomization till death (up to approximately 52 months), Serious adverse events and non-serious adverse events were collected from first dose till 100 days post last dose (Up to approximately 27 months).

Adverse event reporting additional description:

The number at risk for All-Cause mortality represents all randomized participants. The number at risk for serious adverse events and Other (Not Including Serious) adverse events represents all participants that received at least 1 dose of study medication.

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

## Dictionary used

| | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 27.0 |

## Reporting groups

| | |
|---|---|
| Reporting group title | Nivolumab + Docetaxel + Prednisone |

Reporting group description:

Participants with metastatic castration resistant prostate cancer (mCRPC) who are chemotherapy-naïve for mCRPC and have received at least 1 but no more than 2 second-generation hormonal manipulations received Docetaxel 75 milligram per meter square (mg/m^2) intravenous (IV) once in a week (Q3W) + Prednisone 5 milligram (mg) orally (PO) twice a day (BID) + Nivolumab 360 mg IV Q3W for maximum 10 cycles, followed by Nivolumab 480 mg IV once in four weeks (Q4W) until disease progression or unacceptable toxicity or maximum of 2 years from the date of first dose or withdraw of consent.

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

Reporting group description:

Participants with metastatic castration resistant prostate cancer (mCRPC) who are chemotherapy-naïve for mCRPC and have received at least 1 but no more than 2 second-generation hormonal manipulations received Docetaxel 75 mg/m^2 IV Q3W + Prednisone 5 mg PO BID + Placebo IV Q3W for maximum 10 cycles, followed by Placebo IV Q4W until disease progression or unacceptable toxicity or maximum of 2 years from the date of first dose or withdraw of consent.

| **Serious adverse events** | Nivolumab + Docetaxel + Prednisone | Placebo + Docetaxel + Prednisone | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 256 / 510 (50.20%) | 242 / 510 (47.45%) | |
| number of deaths (all causes) | 258 | 227 | |
| number of deaths resulting from adverse events | 79 | 76 | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Brain cancer metastatic | | | |
| subjects affected / exposed | 0 / 510 (0.00%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Acute myeloid leukaemia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 510 (0.00%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bladder cancer | | | |
| subjects affected / exposed | 0 / 510 (0.00%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bladder transitional cell carcinoma | | | |
| subjects affected / exposed | 0 / 510 (0.00%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bronchial neoplasm | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 0 / 510 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Tumour pain | | | |
| subjects affected / exposed | 0 / 510 (0.00%) | 2 / 510 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Colorectal cancer | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 0 / 510 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ependymoma | | | |
| subjects affected / exposed | 0 / 510 (0.00%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Malignant neoplasm progression | | | |
| subjects affected / exposed | 19 / 510 (3.73%) | 27 / 510 (5.29%) | |
| occurrences causally related to treatment / all | 0 / 19 | 0 / 27 | |
| deaths causally related to treatment / all | 0 / 18 | 0 / 22 | |
| Metastases to central nervous system | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 510 (0.00%) | 2 / 510 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metastases to meninges | | | |
| subjects affected / exposed | 2 / 510 (0.39%) | 0 / 510 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Metastases to spine | | | |
| subjects affected / exposed | 0 / 510 (0.00%) | 2 / 510 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metastatic neoplasm | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 0 / 510 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Neoplasm malignant | | | |
| subjects affected / exposed | 0 / 510 (0.00%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Neuroendocrine carcinoma of the skin | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 0 / 510 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Papillary thyroid cancer | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 0 / 510 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Prostate cancer | | | |
| subjects affected / exposed | 10 / 510 (1.96%) | 13 / 510 (2.55%) | |
| occurrences causally related to treatment / all | 0 / 10 | 0 / 13 | |
| deaths causally related to treatment / all | 0 / 10 | 0 / 12 | |
| Squamous cell carcinoma of lung | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 510 (0.00%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Tongue neoplasm | | | |
| subjects affected / exposed | 0 / 510 (0.00%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Tumour associated fever | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 0 / 510 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cancer pain | | | |
| subjects affected / exposed | 3 / 510 (0.59%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Vascular disorders | | | |
| Deep vein thrombosis | | | |
| subjects affected / exposed | 3 / 510 (0.59%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 1 / 3 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Aortic dissection | | | |
| subjects affected / exposed | 0 / 510 (0.00%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haematoma | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 0 / 510 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypertension | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 0 / 510 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Embolism | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 3 / 510 (0.59%) | 3 / 510 (0.59%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Hypotension | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypovolaemic shock | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Venous thrombosis limb | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 0 / 510 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Peripheral arterial occlusive disease | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 0 / 510 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Peripheral ischaemia | | | |
| subjects affected / exposed | 0 / 510 (0.00%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Thrombophlebitis | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 0 / 510 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General disorders and administration site conditions | | | |
| Disease progression | | | |
| subjects affected / exposed | 2 / 510 (0.39%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 2 | 0 / 1 | |
| Asthenia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 3 / 510 (0.59%) | 5 / 510 (0.98%) | |
| occurrences causally related to treatment / all | 1 / 3 | 2 / 6 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Chest discomfort | | | |
| subjects affected / exposed | 0 / 510 (0.00%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Chest pain | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Death | | | |
| subjects affected / exposed | 9 / 510 (1.76%) | 4 / 510 (0.78%) | |
| occurrences causally related to treatment / all | 0 / 9 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 9 | 0 / 4 | |
| Fatigue | | | |
| subjects affected / exposed | 2 / 510 (0.39%) | 3 / 510 (0.59%) | |
| occurrences causally related to treatment / all | 2 / 2 | 1 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Malaise | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 0 / 510 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Mucosal inflammation | | | |
| subjects affected / exposed | 0 / 510 (0.00%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Multiple organ dysfunction syndrome | | | |
| subjects affected / exposed | 2 / 510 (0.39%) | 2 / 510 (0.39%) | |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 2 | |
| deaths causally related to treatment / all | 1 / 1 | 0 / 2 | |
| Oedema peripheral | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 510 (0.20%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pain | | | |
| subjects affected / exposed | 3 / 510 (0.59%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Performance status decreased | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 0 / 510 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pyrexia | | | |
| subjects affected / exposed | 7 / 510 (1.37%) | 3 / 510 (0.59%) | |
| occurrences causally related to treatment / all | 3 / 7 | 2 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sudden death | | | |
| subjects affected / exposed | 2 / 510 (0.39%) | 4 / 510 (0.78%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 2 | 0 / 4 | |
| General physical health deterioration | | | |
| subjects affected / exposed | 3 / 510 (0.59%) | 8 / 510 (1.57%) | |
| occurrences causally related to treatment / all | 0 / 5 | 1 / 9 | |
| deaths causally related to treatment / all | 0 / 2 | 0 / 2 | |
| Immune system disorders | | | |
| Anaphylactic shock | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 0 / 510 (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 | | | |
| Pelvic pain | | | |
| subjects affected / exposed | 0 / 510 (0.00%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|---|---|---|
| Prostatitis | | | |
| subjects affected / exposed | 0 / 510 (0.00%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Interstitial lung disease | | | |
| subjects affected / exposed | 5 / 510 (0.98%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 5 / 5 | 1 / 1 | |
| deaths causally related to treatment / all | 1 / 1 | 0 / 0 | |
| Immune-mediated lung disease | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 0 / 510 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Epistaxis | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 0 / 510 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dyspnoea | | | |
| subjects affected / exposed | 4 / 510 (0.78%) | 7 / 510 (1.37%) | |
| occurrences causally related to treatment / all | 3 / 4 | 5 / 8 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Cough | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Chronic obstructive pulmonary disease | | | |
| subjects affected / exposed | 2 / 510 (0.39%) | 0 / 510 (0.00%) | |
| occurrences causally related to treatment / all | 2 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lung infiltration | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 0 / 510 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|---|---|---|
| Pleural effusion | | | |
| subjects affected / exposed | 0 / 510 (0.00%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory tract haemorrhage | | | |
| subjects affected / exposed | 0 / 510 (0.00%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory failure | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 3 / 510 (0.59%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 2 | |
| Pulmonary oedema | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 0 / 510 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pulmonary embolism | | | |
| subjects affected / exposed | 6 / 510 (1.18%) | 8 / 510 (1.57%) | |
| occurrences causally related to treatment / all | 1 / 6 | 3 / 8 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Pneumothorax | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 2 / 510 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonitis | | | |
| subjects affected / exposed | 13 / 510 (2.55%) | 3 / 510 (0.59%) | |
| occurrences causally related to treatment / all | 13 / 14 | 3 / 3 | |
| deaths causally related to treatment / all | 1 / 1 | 0 / 0 | |
| Psychiatric disorders | | | |
| Delirium | | | |
| subjects affected / exposed | 0 / 510 (0.00%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Adjustment disorder with anxiety | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 510 (0.00%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Anxiety | | | |
| subjects affected / exposed | 0 / 510 (0.00%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Confusional state | | | |
| subjects affected / exposed | 0 / 510 (0.00%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Mental disorder | | | |
| subjects affected / exposed | 0 / 510 (0.00%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Product issues | | | |
| Device dislocation | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 0 / 510 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Device occlusion | | | |
| subjects affected / exposed | 0 / 510 (0.00%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Needle issue | | | |
| subjects affected / exposed | 0 / 510 (0.00%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Investigations | | | |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 0 / 510 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Aspartate aminotransferase | | | |

| | | | |
|---|---|---|---|
| increased | | | |
| subjects affected / exposed | 2 / 510 (0.39%) | 0 / 510 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Blood creatine phosphokinase increased | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 0 / 510 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Blood creatinine increased | | | |
| subjects affected / exposed | 2 / 510 (0.39%) | 0 / 510 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Eastern Cooperative Oncology Group performance status worsened | | | |
| subjects affected / exposed | 0 / 510 (0.00%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General physical condition abnormal | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 3 / 510 (0.59%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatitis B DNA assay positive | | | |
| subjects affected / exposed | 0 / 510 (0.00%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Neutrophil count decreased | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 2 / 510 (0.39%) | |
| occurrences causally related to treatment / all | 1 / 1 | 2 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Platelet count decreased | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Weight decreased | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 510 (0.20%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| White blood cell count decreased | | | |
| subjects affected / exposed | 0 / 510 (0.00%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Injury, poisoning and procedural complications | | | |
| Ankle fracture | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 0 / 510 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Acetabulum fracture | | | |
| subjects affected / exposed | 0 / 510 (0.00%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Fall | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 2 / 510 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Chemical peritonitis | | | |
| subjects affected / exposed | 0 / 510 (0.00%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Concussion | | | |
| subjects affected / exposed | 0 / 510 (0.00%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Femoral neck fracture | | | |
| subjects affected / exposed | 0 / 510 (0.00%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Femur fracture | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 2 / 510 (0.39%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hip fracture | | | |
| subjects affected / exposed | 0 / 510 (0.00%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infusion related reaction | | | |
| subjects affected / exposed | 0 / 510 (0.00%) | 2 / 510 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Limb injury | | | |
| subjects affected / exposed | 0 / 510 (0.00%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lumbar vertebral fracture | | | |
| subjects affected / exposed | 0 / 510 (0.00%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Muscle rupture | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 0 / 510 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pelvic fracture | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 0 / 510 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Rib fracture | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Road traffic accident | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 2 / 510 (0.39%) | 0 / 510 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Skin laceration | | | |
| subjects affected / exposed | 0 / 510 (0.00%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Spinal compression fracture | | | |
| subjects affected / exposed | 0 / 510 (0.00%) | 2 / 510 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Spinal cord injury | | | |
| subjects affected / exposed | 0 / 510 (0.00%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Spinal fracture | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 0 / 510 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Subdural haematoma | | | |
| subjects affected / exposed | 0 / 510 (0.00%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Wound dehiscence | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 0 / 510 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Thoracic vertebral fracture | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 0 / 510 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| **Cardiac disorders** | | | |
| Acute myocardial infarction | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 510 (0.20%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Angina unstable | | | |
| subjects affected / exposed | 0 / 510 (0.00%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Arrhythmia | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 0 / 510 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardio-respiratory arrest | | | |
| subjects affected / exposed | 3 / 510 (0.59%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 3 | 0 / 1 | |
| Atrial flutter | | | |
| subjects affected / exposed | 0 / 510 (0.00%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Atrioventricular block complete | | | |
| subjects affected / exposed | 0 / 510 (0.00%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac arrest | | | |
| subjects affected / exposed | 0 / 510 (0.00%) | 3 / 510 (0.59%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 3 | |
| Cardiac failure | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 5 / 510 (0.98%) | |
| occurrences causally related to treatment / all | 0 / 1 | 4 / 9 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 3 | |
| Cardiac failure congestive | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 2 / 510 (0.39%) | 0 / 510 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Atrial fibrillation | | | |
| subjects affected / exposed | 3 / 510 (0.59%) | 2 / 510 (0.39%) | |
| occurrences causally related to treatment / all | 1 / 4 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiogenic shock | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 0 / 510 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Left ventricular dysfunction | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 0 / 510 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Myocardial infarction | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 0 / 510 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Myocardial ischaemia | | | |
| subjects affected / exposed | 0 / 510 (0.00%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Myocarditis | | | |
| subjects affected / exposed | 0 / 510 (0.00%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Supraventricular tachycardia | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 2 / 510 (0.39%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Immune-mediated myocarditis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 510 (0.20%) | 0 / 510 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 1 / 1 | 0 / 0 | |
| Nervous system disorders | | | |
| Hemiparesis | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 0 / 510 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Headache | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 0 / 510 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Loss of consciousness | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 0 / 510 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Malignant spinal cord compression | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Amnesia | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 0 / 510 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Balance disorder | | | |
| subjects affected / exposed | 0 / 510 (0.00%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Basal ganglia stroke | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 0 / 510 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cauda equina syndrome | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 510 (0.20%) | 0 / 510 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Central nervous system lesion | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 0 / 510 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cerebral haemorrhage | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 0 / 510 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cerebral infarction | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cerebrovascular accident | | | |
| subjects affected / exposed | 5 / 510 (0.98%) | 2 / 510 (0.39%) | |
| occurrences causally related to treatment / all | 1 / 5 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Cognitive disorder | | | |
| subjects affected / exposed | 0 / 510 (0.00%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dizziness | | | |
| subjects affected / exposed | 0 / 510 (0.00%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Embolic stroke | | | |
| subjects affected / exposed | 0 / 510 (0.00%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Guillain-Barre syndrome | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 510 (0.20%) | 0 / 510 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 1 / 1 | 0 / 0 | |
| Ischaemic stroke | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 0 / 510 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nerve compression | | | |
| subjects affected / exposed | 0 / 510 (0.00%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Neuropathy peripheral | | | |
| subjects affected / exposed | 0 / 510 (0.00%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Peripheral sensory neuropathy | | | |
| subjects affected / exposed | 0 / 510 (0.00%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Presyncope | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 0 / 510 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Radiculopathy | | | |
| subjects affected / exposed | 0 / 510 (0.00%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Spinal cord compression | | | |
| subjects affected / exposed | 6 / 510 (1.18%) | 6 / 510 (1.18%) | |
| occurrences causally related to treatment / all | 0 / 6 | 0 / 6 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Superior sagittal sinus thrombosis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 510 (0.00%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Syncope | | | |
| subjects affected / exposed | 2 / 510 (0.39%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 2 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Neuralgia | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 0 / 510 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 6 / 510 (1.18%) | 12 / 510 (2.35%) | |
| occurrences causally related to treatment / all | 4 / 8 | 8 / 14 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Blood disorder | | | |
| subjects affected / exposed | 0 / 510 (0.00%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Bone marrow infiltration | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 0 / 510 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lymphadenitis | | | |
| subjects affected / exposed | 0 / 510 (0.00%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Febrile bone marrow aplasia | | | |
| subjects affected / exposed | 0 / 510 (0.00%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Febrile neutropenia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 17 / 510 (3.33%) | 14 / 510 (2.75%) | |
| occurrences causally related to treatment / all | 16 / 18 | 10 / 16 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Leukopenia | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 3 / 510 (0.59%) | |
| occurrences causally related to treatment / all | 1 / 1 | 3 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Disseminated intravascular coagulation | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Myelosuppression | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 1 / 1 | 2 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Neutropenia | | | |
| subjects affected / exposed | 9 / 510 (1.76%) | 10 / 510 (1.96%) | |
| occurrences causally related to treatment / all | 9 / 9 | 13 / 13 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Thrombocytopenia | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 3 / 510 (0.59%) | |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Eye disorders | | | |
| Cataract | | | |
| subjects affected / exposed | 0 / 510 (0.00%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| Colitis | | | |
| subjects affected / exposed | 4 / 510 (0.78%) | 0 / 510 (0.00%) | |
| occurrences causally related to treatment / all | 3 / 4 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|---|---|---|
| Abdominal pain | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 2 / 510 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Abdominal pain upper | | | |
| subjects affected / exposed | 0 / 510 (0.00%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Anal fistula | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 0 / 510 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Constipation | | | |
| subjects affected / exposed | 2 / 510 (0.39%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 1 / 2 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Large intestine perforation | | | |
| subjects affected / exposed | 0 / 510 (0.00%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diarrhoea | | | |
| subjects affected / exposed | 12 / 510 (2.35%) | 9 / 510 (1.76%) | |
| occurrences causally related to treatment / all | 11 / 12 | 7 / 9 | |
| deaths causally related to treatment / all | 1 / 1 | 0 / 0 | |
| Diverticulum | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 0 / 510 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Duodenal ulcer | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 0 / 510 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Duodenal ulcer haemorrhage | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 510 (0.20%) | 0 / 510 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dysphagia | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Enterocolitis | | | |
| subjects affected / exposed | 2 / 510 (0.39%) | 0 / 510 (0.00%) | |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastric ulcer | | | |
| subjects affected / exposed | 0 / 510 (0.00%) | 2 / 510 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal inflammation | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 0 / 510 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal necrosis | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 0 / 510 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ileus paralytic | | | |
| subjects affected / exposed | 0 / 510 (0.00%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Inguinal hernia | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Intestinal ischaemia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 510 (0.20%) | 0 / 510 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Intestinal obstruction | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Cyclic vomiting syndrome | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 0 / 510 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Large intestine polyp | | | |
| subjects affected / exposed | 0 / 510 (0.00%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lower gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Nausea | | | |
| subjects affected / exposed | 2 / 510 (0.39%) | 3 / 510 (0.59%) | |
| occurrences causally related to treatment / all | 0 / 2 | 2 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Oesophagitis haemorrhagic | | | |
| subjects affected / exposed | 0 / 510 (0.00%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pancreatitis | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 0 / 510 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pancreatitis acute | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 510 (0.20%) | 0 / 510 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Peptic ulcer haemorrhage | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 0 / 510 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Rectal haemorrhage | | | |
| subjects affected / exposed | 0 / 510 (0.00%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Small intestinal obstruction | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 0 / 510 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Subileus | | | |
| subjects affected / exposed | 0 / 510 (0.00%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Upper gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 2 / 510 (0.39%) | 0 / 510 (0.00%) | |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vomiting | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 3 / 510 (0.59%) | |
| occurrences causally related to treatment / all | 0 / 1 | 2 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Leukoplakia oral | | | |
| subjects affected / exposed | 0 / 510 (0.00%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatobiliary disorders | | | |
| Hepatic function abnormal | | | |

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|---|---|---|---|
| subjects affected / exposed | 0 / 510 (0.00%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Acute cholecystitis necrotic | | | |
| subjects affected / exposed | 0 / 510 (0.00%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Autoimmune hepatitis | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 0 / 510 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Biliary dilatation | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 0 / 510 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cholangitis | | | |
| subjects affected / exposed | 2 / 510 (0.39%) | 0 / 510 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cholecystitis acute | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 0 / 510 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatitis toxic | | | |
| subjects affected / exposed | 0 / 510 (0.00%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Immune-mediated hepatitis | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 0 / 510 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 1 / 1 | 0 / 0 | |
| Liver injury | | | |

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|---|---|---|---|
| subjects affected / exposed | 1 / 510 (0.20%) | 0 / 510 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hyperbilirubinaemia | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 0 / 510 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Skin and subcutaneous tissue disorders | | | |
| Skin ulcer | | | |
| subjects affected / exposed | 0 / 510 (0.00%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Skin disorder | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 0 / 510 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pemphigoid | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 0 / 510 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal and urinary disorders | | | |
| Acute kidney injury | | | |
| subjects affected / exposed | 4 / 510 (0.78%) | 5 / 510 (0.98%) | |
| occurrences causally related to treatment / all | 2 / 4 | 1 / 6 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Calculus bladder | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 0 / 510 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Calculus urethral | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 0 / 510 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Chronic kidney disease | | | |

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|---|---|---|---|
| subjects affected / exposed | 2 / 510 (0.39%) | 0 / 510 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dysuria | | | |
| subjects affected / exposed | 2 / 510 (0.39%) | 0 / 510 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haematuria | | | |
| subjects affected / exposed | 13 / 510 (2.55%) | 2 / 510 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 19 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Hydronephrosis | | | |
| subjects affected / exposed | 0 / 510 (0.00%) | 2 / 510 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Immune-mediated nephritis | | | |
| subjects affected / exposed | 0 / 510 (0.00%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nephritis | | | |
| subjects affected / exposed | 0 / 510 (0.00%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nephrolithiasis | | | |
| subjects affected / exposed | 0 / 510 (0.00%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal colic | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 0 / 510 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal failure | | | |

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|---|---|---|---|
| subjects affected / exposed | 0 / 510 (0.00%) | 2 / 510 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urethral obstruction | | | |
| subjects affected / exposed | 0 / 510 (0.00%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urinary tract obstruction | | | |
| subjects affected / exposed | 2 / 510 (0.39%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urinary tract inflammation | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 0 / 510 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urinary retention | | | |
| subjects affected / exposed | 2 / 510 (0.39%) | 4 / 510 (0.78%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Endocrine disorders | | | |
| Adrenal insufficiency | | | |
| subjects affected / exposed | 2 / 510 (0.39%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 2 / 2 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hyperthyroidism | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 0 / 510 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypothyroidism | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Immune-mediated hypophysitis | | | |

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|---|---|---|---|
| subjects affected / exposed | 1 / 510 (0.20%) | 0 / 510 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Inappropriate antidiuretic hormone secretion | | | |
| subjects affected / exposed | 0 / 510 (0.00%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| **Musculoskeletal and connective tissue disorders** | | | |
| Muscle spasms | | | |
| subjects affected / exposed | 0 / 510 (0.00%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Arthralgia | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 4 / 510 (0.78%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Back pain | | | |
| subjects affected / exposed | 3 / 510 (0.59%) | 8 / 510 (1.57%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 8 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bone pain | | | |
| subjects affected / exposed | 3 / 510 (0.59%) | 5 / 510 (0.98%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 7 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Flank pain | | | |
| subjects affected / exposed | 0 / 510 (0.00%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Immune-mediated arthritis | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 0 / 510 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Immune-mediated myositis | | | |

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|---|---|---|---|
| subjects affected / exposed | 1 / 510 (0.20%) | 0 / 510 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Intervertebral disc protrusion | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 0 / 510 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Muscular weakness | | | |
| subjects affected / exposed | 3 / 510 (0.59%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 1 / 3 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Myalgia | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Myositis | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 0 / 510 (0.00%) | |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Osteonecrosis | | | |
| subjects affected / exposed | 0 / 510 (0.00%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Osteonecrosis of jaw | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 2 / 510 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Osteoporosis | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 0 / 510 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pain in extremity | | | |

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|---|---|---|---|
| subjects affected / exposed | 2 / 510 (0.39%) | 0 / 510 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pain in jaw | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 0 / 510 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pathological fracture | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 4 / 510 (0.78%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Rhabdomyolysis | | | |
| subjects affected / exposed | 0 / 510 (0.00%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sacral pain | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 0 / 510 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Spinal pain | | | |
| subjects affected / exposed | 0 / 510 (0.00%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal pain | | | |
| subjects affected / exposed | 0 / 510 (0.00%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Cellulitis streptococcal | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 0 / 510 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Abdominal infection | | | |

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|---|---|---|---|
| subjects affected / exposed | 0 / 510 (0.00%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Abscess limb | | | |
| subjects affected / exposed | 0 / 510 (0.00%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Anal abscess | | | |
| subjects affected / exposed | 0 / 510 (0.00%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Appendicitis | | | |
| subjects affected / exposed | 0 / 510 (0.00%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Atypical pneumonia | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 0 / 510 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bacteraemia | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bone abscess | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 0 / 510 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bronchiolitis | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 0 / 510 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bronchitis | | | |

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|---|---|---|---|
| subjects affected / exposed | 1 / 510 (0.20%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| COVID-19 | | | |
| subjects affected / exposed | 11 / 510 (2.16%) | 13 / 510 (2.55%) | |
| occurrences causally related to treatment / all | 0 / 11 | 0 / 13 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 2 | |
| COVID-19 pneumonia | | | |
| subjects affected / exposed | 2 / 510 (0.39%) | 3 / 510 (0.59%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 1 | |
| Cellulitis | | | |
| subjects affected / exposed | 4 / 510 (0.78%) | 2 / 510 (0.39%) | |
| occurrences causally related to treatment / all | 2 / 4 | 2 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Coronavirus infection | | | |
| subjects affected / exposed | 0 / 510 (0.00%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Meningitis | | | |
| subjects affected / exposed | 0 / 510 (0.00%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Device related infection | | | |
| subjects affected / exposed | 0 / 510 (0.00%) | 2 / 510 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Device related sepsis | | | |
| subjects affected / exposed | 0 / 510 (0.00%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diarrhoea infectious | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 510 (0.00%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diverticulitis | | | |
| subjects affected / exposed | 3 / 510 (0.59%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 2 / 3 | 0 / 1 | |
| deaths causally related to treatment / all | 2 / 2 | 0 / 0 | |
| Diverticulitis intestinal perforated | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 0 / 510 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Febrile infection | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastroenteritis | | | |
| subjects affected / exposed | 3 / 510 (0.59%) | 0 / 510 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal infection | | | |
| subjects affected / exposed | 0 / 510 (0.00%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infection | | | |
| subjects affected / exposed | 0 / 510 (0.00%) | 2 / 510 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Influenza | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Intervertebral discitis | | | |

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|---|---|---|---|
| subjects affected / exposed | 1 / 510 (0.20%) | 0 / 510 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Klebsiella urinary tract infection | | | |
| subjects affected / exposed | 0 / 510 (0.00%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Liver abscess | | | |
| subjects affected / exposed | 0 / 510 (0.00%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lower respiratory tract infection | | | |
| subjects affected / exposed | 2 / 510 (0.39%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Lung abscess | | | |
| subjects affected / exposed | 0 / 510 (0.00%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cystitis | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 0 / 510 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Neutropenic sepsis | | | |
| subjects affected / exposed | 4 / 510 (0.78%) | 0 / 510 (0.00%) | |
| occurrences causally related to treatment / all | 4 / 4 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Scrotal infection | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 0 / 510 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Osteomyelitis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 510 (0.20%) | 2 / 510 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Perineal abscess | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 0 / 510 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Peritonitis | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 0 / 510 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 1 / 1 | 0 / 0 | |
| Pneumocystis jirovecii pneumonia | | | |
| subjects affected / exposed | 2 / 510 (0.39%) | 2 / 510 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 2 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 1 / 1 | |
| Pneumonia | | | |
| subjects affected / exposed | 18 / 510 (3.53%) | 8 / 510 (1.57%) | |
| occurrences causally related to treatment / all | 9 / 18 | 3 / 9 | |
| deaths causally related to treatment / all | 2 / 4 | 0 / 1 | |
| Pneumonia aspiration | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Pneumonia bacterial | | | |
| subjects affected / exposed | 3 / 510 (0.59%) | 2 / 510 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 2 | |
| Post procedural infection | | | |
| subjects affected / exposed | 0 / 510 (0.00%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Postoperative wound infection | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 510 (0.00%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Psoas abscess | | | |
| subjects affected / exposed | 0 / 510 (0.00%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pulmonary sepsis | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 0 / 510 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal abscess | | | |
| subjects affected / exposed | 0 / 510 (0.00%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory syncytial virus infection | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 0 / 510 (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 | | | |
| subjects affected / exposed | 0 / 510 (0.00%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Scrotal abscess | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 0 / 510 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Oral candidiasis | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sepsis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 7 / 510 (1.37%) | 10 / 510 (1.96%) | |
| occurrences causally related to treatment / all | 3 / 7 | 3 / 11 | |
| deaths causally related to treatment / all | 3 / 4 | 0 / 1 | |
| Sinusitis | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 0 / 510 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Soft tissue infection | | | |
| subjects affected / exposed | 0 / 510 (0.00%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Spinal cord infection | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 0 / 510 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Staphylococcal bacteraemia | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 0 / 510 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Staphylococcal infection | | | |
| subjects affected / exposed | 0 / 510 (0.00%) | 2 / 510 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Staphylococcal sepsis | | | |
| subjects affected / exposed | 0 / 510 (0.00%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Streptococcal infection | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 0 / 510 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Tuberculosis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 510 (0.20%) | 0 / 510 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 0 / 510 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urinary tract infection | | | |
| subjects affected / exposed | 8 / 510 (1.57%) | 10 / 510 (1.96%) | |
| occurrences causally related to treatment / all | 0 / 9 | 0 / 13 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Urosepsis | | | |
| subjects affected / exposed | 2 / 510 (0.39%) | 2 / 510 (0.39%) | |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 2 | |
| deaths causally related to treatment / all | 1 / 1 | 0 / 0 | |
| Vascular device infection | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 2 / 510 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Wound infection staphylococcal | | | |
| subjects affected / exposed | 0 / 510 (0.00%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Septic shock | | | |
| subjects affected / exposed | 0 / 510 (0.00%) | 5 / 510 (0.98%) | |
| occurrences causally related to treatment / all | 0 / 0 | 4 / 6 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Metabolism and nutrition disorders | | | |
| Diabetic ketoacidosis | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 0 / 510 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Decreased appetite | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 3 / 510 (0.59%) | 2 / 510 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dehydration | | | |
| subjects affected / exposed | 2 / 510 (0.39%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diabetes mellitus | | | |
| subjects affected / exposed | 0 / 510 (0.00%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Failure to thrive | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 0 / 510 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hyperglycaemia | | | |
| subjects affected / exposed | 0 / 510 (0.00%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypernatraemia | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 0 / 510 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypokalaemia | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 1 / 510 (0.20%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hyponatraemia | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 4 / 510 (0.78%) | |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ketoacidosis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 510 (0.20%) | 0 / 510 (0.00%) | |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Malnutrition | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 0 / 510 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Type 2 diabetes mellitus | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 0 / 510 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypercalcaemia | | | |
| subjects affected / exposed | 1 / 510 (0.20%) | 0 / 510 (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** | Nivolumab + Docetaxel + Prednisone | Placebo + Docetaxel + Prednisone | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 479 / 510 (93.92%) | 494 / 510 (96.86%) | |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 113 / 510 (22.16%) | 108 / 510 (21.18%) | |
| occurrences (all) | 183 | 148 | |
| Fatigue | | | |
| subjects affected / exposed | 141 / 510 (27.65%) | 149 / 510 (29.22%) | |
| occurrences (all) | 171 | 175 | |
| Pyrexia | | | |
| subjects affected / exposed | 41 / 510 (8.04%) | 54 / 510 (10.59%) | |
| occurrences (all) | 57 | 69 | |
| Pain | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 24 / 510 (4.71%) | 26 / 510 (5.10%) | |
| occurrences (all) | 27 | 27 | |
| Oedema peripheral | | | |
| subjects affected / exposed | 90 / 510 (17.65%) | 108 / 510 (21.18%) | |
| occurrences (all) | 94 | 119 | |
| Mucosal inflammation | | | |
| subjects affected / exposed | 20 / 510 (3.92%) | 30 / 510 (5.88%) | |
| occurrences (all) | 36 | 35 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough | | | |
| subjects affected / exposed | 51 / 510 (10.00%) | 49 / 510 (9.61%) | |
| occurrences (all) | 58 | 51 | |
| Dyspnoea | | | |
| subjects affected / exposed | 52 / 510 (10.20%) | 38 / 510 (7.45%) | |
| occurrences (all) | 56 | 45 | |
| Psychiatric disorders | | | |
| Insomnia | | | |
| subjects affected / exposed | 35 / 510 (6.86%) | 47 / 510 (9.22%) | |
| occurrences (all) | 36 | 53 | |
| Investigations | | | |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 38 / 510 (7.45%) | 16 / 510 (3.14%) | |
| occurrences (all) | 44 | 22 | |
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 27 / 510 (5.29%) | 20 / 510 (3.92%) | |
| occurrences (all) | 32 | 23 | |
| Neutrophil count decreased | | | |
| subjects affected / exposed | 47 / 510 (9.22%) | 46 / 510 (9.02%) | |
| occurrences (all) | 119 | 75 | |
| Weight decreased | | | |
| subjects affected / exposed | 42 / 510 (8.24%) | 42 / 510 (8.24%) | |
| occurrences (all) | 43 | 46 | |
| White blood cell count decreased | | | |
| subjects affected / exposed | 33 / 510 (6.47%) | 39 / 510 (7.65%) | |
| occurrences (all) | 99 | 65 | |
| Injury, poisoning and procedural | | | |

| | | | |
|---|---|---|---|
| complications | | | |
| Infusion related reaction | | | |
| subjects affected / exposed | 22 / 510 (4.31%) | 26 / 510 (5.10%) | |
| occurrences (all) | 24 | 43 | |
| Nervous system disorders | | | |
| Dysgeusia | | | |
| subjects affected / exposed | 59 / 510 (11.57%) | 44 / 510 (8.63%) | |
| occurrences (all) | 74 | 56 | |
| Headache | | | |
| subjects affected / exposed | 29 / 510 (5.69%) | 26 / 510 (5.10%) | |
| occurrences (all) | 32 | 29 | |
| Neuropathy peripheral | | | |
| subjects affected / exposed | 76 / 510 (14.90%) | 75 / 510 (14.71%) | |
| occurrences (all) | 81 | 80 | |
| Peripheral sensory neuropathy | | | |
| subjects affected / exposed | 38 / 510 (7.45%) | 42 / 510 (8.24%) | |
| occurrences (all) | 39 | 43 | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 157 / 510 (30.78%) | 165 / 510 (32.35%) | |
| occurrences (all) | 209 | 207 | |
| Neutropenia | | | |
| subjects affected / exposed | 40 / 510 (7.84%) | 58 / 510 (11.37%) | |
| occurrences (all) | 51 | 90 | |
| Eye disorders | | | |
| Lacrimation increased | | | |
| subjects affected / exposed | 16 / 510 (3.14%) | 28 / 510 (5.49%) | |
| occurrences (all) | 17 | 28 | |
| Gastrointestinal disorders | | | |
| Vomiting | | | |
| subjects affected / exposed | 60 / 510 (11.76%) | 59 / 510 (11.57%) | |
| occurrences (all) | 66 | 73 | |
| Stomatitis | | | |
| subjects affected / exposed | 34 / 510 (6.67%) | 20 / 510 (3.92%) | |
| occurrences (all) | 44 | 26 | |
| Nausea | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 108 / 510 (21.18%) | 134 / 510 (26.27%) | |
| occurrences (all) | 145 | 182 | |
| Diarrhoea | | | |
| subjects affected / exposed | 175 / 510 (34.31%) | 162 / 510 (31.76%) | |
| occurrences (all) | 294 | 244 | |
| Constipation | | | |
| subjects affected / exposed | 112 / 510 (21.96%) | 101 / 510 (19.80%) | |
| occurrences (all) | 133 | 132 | |
| Skin and subcutaneous tissue disorders | | | |
| Nail disorder | | | |
| subjects affected / exposed | 37 / 510 (7.25%) | 41 / 510 (8.04%) | |
| occurrences (all) | 38 | 42 | |
| Alopecia | | | |
| subjects affected / exposed | 172 / 510 (33.73%) | 178 / 510 (34.90%) | |
| occurrences (all) | 172 | 178 | |
| Pruritus | | | |
| subjects affected / exposed | 48 / 510 (9.41%) | 22 / 510 (4.31%) | |
| occurrences (all) | 55 | 27 | |
| Rash | | | |
| subjects affected / exposed | 52 / 510 (10.20%) | 36 / 510 (7.06%) | |
| occurrences (all) | 67 | 38 | |
| Renal and urinary disorders | | | |
| Haematuria | | | |
| subjects affected / exposed | 29 / 510 (5.69%) | 22 / 510 (4.31%) | |
| occurrences (all) | 34 | 23 | |
| Endocrine disorders | | | |
| Hypothyroidism | | | |
| subjects affected / exposed | 29 / 510 (5.69%) | 14 / 510 (2.75%) | |
| occurrences (all) | 33 | 15 | |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 84 / 510 (16.47%) | 97 / 510 (19.02%) | |
| occurrences (all) | 103 | 108 | |
| Back pain | | | |
| subjects affected / exposed | 78 / 510 (15.29%) | 85 / 510 (16.67%) | |
| occurrences (all) | 80 | 92 | |

| | | | |
|---|---|---|---|
| Bone pain | | | |
| subjects affected / exposed | 49 / 510 (9.61%) | 42 / 510 (8.24%) | |
| occurrences (all) | 52 | 47 | |
| Myalgia | | | |
| subjects affected / exposed | 39 / 510 (7.65%) | 51 / 510 (10.00%) | |
| occurrences (all) | 42 | 65 | |
| Pain in extremity | | | |
| subjects affected / exposed | 41 / 510 (8.04%) | 52 / 510 (10.20%) | |
| occurrences (all) | 46 | 61 | |
| Infections and infestations | | | |
| Urinary tract infection | | | |
| subjects affected / exposed | 37 / 510 (7.25%) | 31 / 510 (6.08%) | |
| occurrences (all) | 61 | 48 | |
| COVID-19 | | | |
| subjects affected / exposed | 63 / 510 (12.35%) | 62 / 510 (12.16%) | |
| occurrences (all) | 66 | 63 | |
| Metabolism and nutrition disorders | | | |
| Decreased appetite | | | |
| subjects affected / exposed | 96 / 510 (18.82%) | 97 / 510 (19.02%) | |
| occurrences (all) | 119 | 116 | |
| Hyperglycaemia | | | |
| subjects affected / exposed | 34 / 510 (6.67%) | 43 / 510 (8.43%) | |
| occurrences (all) | 37 | 52 | |
| Hypocalcaemia | | | |
| subjects affected / exposed | 23 / 510 (4.51%) | 29 / 510 (5.69%) | |
| occurrences (all) | 28 | 36 | |

## More information

## Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---|---|
| 17 May 2021 | Removed exclusion criterion for prior radium-223 exposure. Aligned dose modification criteria and immuno-oncology (IO) agent management algorithms with National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE) version 5. Added serologic testing for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) status. Incorporated additional updates in order to improve alignment between protocol sections and clarify remote monitoring, prior malignancy window, thyroid testing, and male contraception requirements. |
| 13 September 2022 | Changes to the statistical analysis section, in which the population for radiographic progression-free survival (rPFS) analysis has been changed from the first 544 participants randomized to all randomized and the number of events from 433 to 530 rPFS events. Changes to clarify censoring rules for rPFS. Increased overall survival (OS) events from 615 to 690. Clarification of pharmacokinetic sampling at follow-up visits. Clarification of SARS-CoV-2 serology at follow-up as optional. |
| 22 September 2023 | The purpose of this protocol amendment is to formally incorporate guidance provided in the "Dear Investigator" letters from 27-Jul-2023 and 10-Aug-2023, and further clarify participant management and study procedures as the study proceeds toward termination due to one of the primary efficacy endpoints not meeting the success criterion and the implausibility of success of the other primary endpoint. The decision to terminate the study was not based on any safety concerns or issues. On 26-Jul-2023 the study independent Data Monitoring Committee convened. Based on a clinical data cutoff of 01-Jun-2023, the addition of nivolumab to docetaxel plus prednisone did not result in a statistically significant improvement in radiographic progression-free survival (rPFS) (hazard ratio 0.96; 99% confidence interval [CI] 0.77, 1.19) at final analysis and overall survival (OS) at the first interim analysis (hazard ratio 1.09; 99.41% CI 0.84, 1.43) compared to placebo added to docetaxel plus prednisone. A Sponsor Executive Oversight Committee (EOC) requested to be unblinded to the study results. Further evaluation of OS results showed no plausible scenario of reaching OS statistical significance at subsequent, planned statistical analyses, including the second interim analysis and final analysis. Given the lack of clinical benefit from nivolumab added to docetaxel plus prednisone for the dual primary efficacy endpoints of rPFS and OS, the Sponsor EOC decided to terminate the study. Unblinding of study treatment assignment to full study teams and investigators occurred on 03-Aug-2023. |

Notes:

## Interruptions (globally)

Were there any global interruptions to the trial? No

## Limitations and caveats

None reported