



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
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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
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Arm title	Nivolumab + Docetaxel + Prednisone
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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/m²) 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
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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/m² 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/m ² 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
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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/m ² 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/m ² 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
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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/m²) 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
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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/m² 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 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 Units: years			
arithmetic mean	68.9	69.6	
standard deviation	± 7.5	± 8.1	-
Sex: Female, Male Units: participants			
Female	0	1	1
Male	514	515	1029
Race/Ethnicity, Customized 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
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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/m²) 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
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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/m² 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
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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/m²) 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
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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/m² 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)
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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
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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: 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)
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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
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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: 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: 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)
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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
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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: Time to PSA Progression (TTP-PSA)

End point title	Time to PSA Progression (TTP-PSA)
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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: 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: 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 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 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 Adverse Events Leading to Discontinuation

End point title	Number of Participants with Adverse Events Leading to Discontinuation
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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
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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
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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
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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		
Hypertransaminaemia	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
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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
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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 erythrodysesthesia 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
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End point description:

End point type	Secondary
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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
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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
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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
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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
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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)
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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
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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		

Statistical analyses

No statistical analyses for this end point

Adverse events

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
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	27.0
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Reporting groups

Reporting group title	Nivolumab + Docetaxel + Prednisone
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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/m²) 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
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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/m² 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			

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			

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			

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			

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			

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			

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			

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			

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			

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			

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 occurrences (all)	24 / 510 (4.71%) 27	26 / 510 (5.10%) 27	
Oedema peripheral subjects affected / exposed occurrences (all)	90 / 510 (17.65%) 94	108 / 510 (21.18%) 119	
Mucosal inflammation subjects affected / exposed occurrences (all)	20 / 510 (3.92%) 36	30 / 510 (5.88%) 35	
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	51 / 510 (10.00%) 58	49 / 510 (9.61%) 51	
Dyspnoea subjects affected / exposed occurrences (all)	52 / 510 (10.20%) 56	38 / 510 (7.45%) 45	
Psychiatric disorders Insomnia subjects affected / exposed occurrences (all)	35 / 510 (6.86%) 36	47 / 510 (9.22%) 53	
Investigations Alanine aminotransferase increased subjects affected / exposed occurrences (all)	38 / 510 (7.45%) 44	16 / 510 (3.14%) 22	
Aspartate aminotransferase increased subjects affected / exposed occurrences (all)	27 / 510 (5.29%) 32	20 / 510 (3.92%) 23	
Neutrophil count decreased subjects affected / exposed occurrences (all)	47 / 510 (9.22%) 119	46 / 510 (9.02%) 75	
Weight decreased subjects affected / exposed occurrences (all)	42 / 510 (8.24%) 43	42 / 510 (8.24%) 46	
White blood cell count decreased subjects affected / exposed occurrences (all)	33 / 510 (6.47%) 99	39 / 510 (7.65%) 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 occurrences (all)	49 / 510 (9.61%) 52	42 / 510 (8.24%) 47	
Myalgia subjects affected / exposed occurrences (all)	39 / 510 (7.65%) 42	51 / 510 (10.00%) 65	
Pain in extremity subjects affected / exposed occurrences (all)	41 / 510 (8.04%) 46	52 / 510 (10.20%) 61	
Infections and infestations Urinary tract infection subjects affected / exposed occurrences (all)	37 / 510 (7.25%) 61	31 / 510 (6.08%) 48	
COVID-19 subjects affected / exposed occurrences (all)	63 / 510 (12.35%) 66	62 / 510 (12.16%) 63	
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	96 / 510 (18.82%) 119	97 / 510 (19.02%) 116	
Hyperglycaemia subjects affected / exposed occurrences (all)	34 / 510 (6.67%) 37	43 / 510 (8.43%) 52	
Hypocalcaemia subjects affected / exposed occurrences (all)	23 / 510 (4.51%) 28	29 / 510 (5.69%) 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