



Clinical trial results:

An Open-label Randomized Phase III Trial of BMS-936558 (Nivolumab) versus Docetaxel in Previously Treated Advanced or Metastatic Squamous Cell Non-small Cell Lung Cancer (NSCLC) (CheckMate 017: CHECKpoint pathway and nivoluMAb clinical Trial Evaluation 017)

Summary

EudraCT number	2011-004792-36
Trial protocol	IE DE NL GB IT ES AT HU CZ NO PL
Global end of trial date	16 August 2021

Results information

Result version number	v1 (current)
This version publication date	01 September 2022
First version publication date	01 September 2022

Trial information

Trial identification

Sponsor protocol code	CA209-017
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Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Bristol-Myers Squibb
Sponsor organisation address	Chaussee de la Hulpe 185, Brussels, Belgium, 1170
Public contact	EU Study Start-Up Unit, Bristol-Myers Squibb International Corporation, Clinical.Trials@bms.com
Scientific contact	Bristol-Myers Squibb Study Director, Bristol-Myers Squibb, Clinical.Trials@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	13 October 2021
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	16 August 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

BMS-936558 (nivolumab) increases OS as compared with docetaxel, in squamous cell NSCLC subjects treated with prior platinum doublet-based chemotherapy.

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	12 October 2012
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 8
Country: Number of subjects enrolled	Australia: 5
Country: Number of subjects enrolled	Austria: 3
Country: Number of subjects enrolled	Canada: 2
Country: Number of subjects enrolled	Chile: 8
Country: Number of subjects enrolled	Czechia: 5
Country: Number of subjects enrolled	France: 17
Country: Number of subjects enrolled	Germany: 16
Country: Number of subjects enrolled	Hungary: 2
Country: Number of subjects enrolled	Ireland: 2
Country: Number of subjects enrolled	Italy: 14
Country: Number of subjects enrolled	Mexico: 8
Country: Number of subjects enrolled	Netherlands: 13
Country: Number of subjects enrolled	Norway: 4
Country: Number of subjects enrolled	Peru: 2
Country: Number of subjects enrolled	Poland: 17
Country: Number of subjects enrolled	Romania: 11
Country: Number of subjects enrolled	Russian Federation: 20
Country: Number of subjects enrolled	Spain: 22
Country: Number of subjects enrolled	United Kingdom: 9

Country: Number of subjects enrolled	United States: 84
Worldwide total number of subjects	272
EEA total number of subjects	126

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)	152
From 65 to 84 years	119
85 years and over	1

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

272 participants were randomized and 260 received treatment

Period 1

Period 1 title	Randomization
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Nivolumab

Arm description:

Nivolumab 3 mg/kg solution intravenously every 2 weeks until documented disease progression, discontinuation due to toxicity, withdrawal of consent or the study ends. Eligible patients may receive nivolumab at 480mg every 4 weeks until documented disease progression, discontinuation, withdrawal of consent or the study ends.

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:

Nivolumab 3 mg/kg solution intravenously every 2 weeks

Investigational medicinal product name	Nivolumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Nivolumab at 480mg every 4 weeks

Arm title	Docetaxel
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Arm description:

Docetaxel 75mg/m² solution intravenously every 3 weeks until documented disease progression , discontinuation due to toxicity, withdrawal of consent or study ends. Eligible patients may receive nivolumab 3 mg/kg every 2 weeks and/or nivolumab 480 mg flat dose every 4 weeks via extension phase until documented disease progression, discontinuation due to toxicity, withdrawal of consent or study ends.

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:

Nivolumab at 480mg every 4 weeks

Investigational medicinal product name	Docetaxel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for concentrate for solution for infusion, Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Docetaxel 75 mg/m² solution intravenously every 3 weeks

Number of subjects in period 1	Nivolumab	Docetaxel
Started	135	137
Completed	131	129
Not completed	4	8
Adverse Event unrelated to study drug	1	-
Participant withdrew consent	1	6
No longer meets study criteria	2	2

Period 2

Period 2 title	Transition to Nivolumab
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Nivolumab

Arm description:

Nivolumab 3 mg/kg solution intravenously every 2 weeks until documented disease progression, discontinuation due to toxicity, withdrawal of consent or the study ends. Eligible patients may receive nivolumab at 480mg every 4 weeks until documented disease progression, discontinuation, withdrawal of consent or the study ends.

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:

Nivolumab at 480mg every 4 weeks

Investigational medicinal product name	Nivolumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Nivolumab 3 mg/kg solution intravenously every 2 weeks

Arm title	Docetaxel
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Arm description:

Docetaxel 75mg/m² solution intravenously every 3 weeks until documented disease progression , discontinuation due to toxicity, withdrawal of consent or study ends. Eligible patients may receive nivolumab 3 mg/kg every 2 weeks and/or nivolumab 480 mg flat dose every 4 weeks via extension phase until documented disease progression, discontinuation due to toxicity, withdrawal of consent or study ends.

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:

Nivolumab at 480mg every 4 weeks

Investigational medicinal product name	Docetaxel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for concentrate for solution for infusion, Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Docetaxel 75 mg/m² solution intravenously every 3 weeks

Number of subjects in period 2	Nivolumab	Docetaxel
Started	131	129
Subjects transitioned to Nivolumab	0	6
Completed	0	0
Not completed	131	129
Adverse event, serious fatal	1	1
Subject withdrew consent	5	5
Adverse Event unrelated to study drug	9	13
Disease progression	95	79
Study drug toxicity	10	13
Subject request to discontinue study treatment	6	4
Not reported	-	3
Maximum clinical benefit	1	9
Other reasons	2	-
Poor/Non-compliance	1	-

No longer meets study criteria	1	2
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Baseline characteristics

Reporting groups

Reporting group title	Nivolumab
Reporting group description:	
Nivolumab 3 mg/kg solution intravenously every 2 weeks until documented disease progression, discontinuation due to toxicity, withdrawal of consent or the study ends. Eligible patients may receive nivolumab at 480mg every 4 weeks until documented disease progression, discontinuation, withdrawal of consent or the study ends.	
Reporting group title	Docetaxel
Reporting group description:	
Docetaxel 75mg/m ² solution intravenously every 3 weeks until documented disease progression , discontinuation due to toxicity, withdrawal of consent or study ends. Eligible patients may receive nivolumab 3 mg/kg every 2 weeks and/or nivolumab 480 mg flat dose every 4 weeks via extension phase until documented disease progression, discontinuation due to toxicity, withdrawal of consent or study ends.	

Reporting group values	Nivolumab	Docetaxel	Total
Number of subjects	135	137	272
Age Categorical Units: Participants			
< 65 years	79	73	152
>= 65 AND < 75 years	45	46	91
>= 75 AND < 85 years	10	18	28
>= 85 years	1	0	1
<= 18 years	0	0	0
Age Continuous Units: years			
arithmetic mean	62.2	64.4	
standard deviation	± 8.33	± 8.28	-
Sex: Female, Male Units:			
Female	24	40	64
Male	111	97	208
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	7	5	12
Not Hispanic or Latino	61	60	121
Unknown or Not Reported	67	72	139
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	4	2	6
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	6	2	8
White	122	130	252
More than one race	0	0	0
Unknown or Not Reported	3	3	6

End points

End points reporting groups

Reporting group title	Nivolumab
Reporting group description: Nivolumab 3 mg/kg solution intravenously every 2 weeks until documented disease progression, discontinuation due to toxicity, withdrawal of consent or the study ends. Eligible patients may receive nivolumab at 480mg every 4 weeks until documented disease progression, discontinuation, withdrawal of consent or the study ends.	
Reporting group title	Docetaxel
Reporting group description: Docetaxel 75mg/m ² solution intravenously every 3 weeks until documented disease progression , discontinuation due to toxicity, withdrawal of consent or study ends. Eligible patients may receive nivolumab 3 mg/kg every 2 weeks and/or nivolumab 480 mg flat dose every 4 weeks via extension phase until documented disease progression, discontinuation due to toxicity, withdrawal of consent or study ends.	
Reporting group title	Nivolumab
Reporting group description: Nivolumab 3 mg/kg solution intravenously every 2 weeks until documented disease progression, discontinuation due to toxicity, withdrawal of consent or the study ends. Eligible patients may receive nivolumab at 480mg every 4 weeks until documented disease progression, discontinuation, withdrawal of consent or the study ends.	
Reporting group title	Docetaxel
Reporting group description: Docetaxel 75mg/m ² solution intravenously every 3 weeks until documented disease progression , discontinuation due to toxicity, withdrawal of consent or study ends. Eligible patients may receive nivolumab 3 mg/kg every 2 weeks and/or nivolumab 480 mg flat dose every 4 weeks via extension phase until documented disease progression, discontinuation due to toxicity, withdrawal of consent or study ends.	

Primary: Overall Survival (OS) Rate in All Randomized Participants

End point title	Overall Survival (OS) Rate in All Randomized Participants ^[1]
End point description: The overall survival rate is the probability that a participant will be alive at 6, 12, and 18 months following randomization. Overall survival was defined as the time between the date of randomization and the date of death as a result of any cause. Survival rates were determined via Kaplan-Meier estimates.	
End point type	Primary
End point timeframe: Randomization to 18 months post-randomization, up to June 2015	
Notes: [1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point. Justification: Only summary statistics were planned for this endpoint	

End point values	Nivolumab	Docetaxel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	135	137		
Units: Percent probability of OS				
number (confidence interval 95%)				
6 months	63.7 (55.0 to 71.2)	50.7 (42.1 to 58.8)		
12 months	42.2 (33.8 to 50.4)	24.3 (17.4 to 31.7)		

18 months	28.1 (20.8 to 35.8)	12.5 (7.6 to 18.7)		
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Statistical analyses

No statistical analyses for this end point

Primary: Number of Deaths From Any Cause in All Randomized Participants at Primary Endpoint

End point title	Number of Deaths From Any Cause in All Randomized Participants at Primary Endpoint ^[2]
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End point description:

The number of participants who died from any cause was reported for each arm. Interim analysis (Primary Endpoint) was planned to occur after at least 196 deaths, with the actual analysis occurring at 199 deaths.

End point type	Primary
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End point timeframe:

Randomization until 199 deaths, up to November 2014, approximately 25 months

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Only summary statistics were planned for this endpoint

End point values	Nivolumab	Docetaxel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	135	137		
Units: Participants	86	113		

Statistical analyses

No statistical analyses for this end point

Primary: Overall Survival (OS) Time in Months for All Randomized Participants at Primary Endpoint

End point title	Overall Survival (OS) Time in Months for All Randomized Participants at Primary Endpoint
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End point description:

OS was defined as the time between the date of randomization and the date of death from any cause. Participants were censored at the date they were last known to be alive. Median OS time was calculated using Kaplan-Meier (KM) method. Hazard ratio (HR) and the corresponding Confidence Interval (CI) were estimated in a stratified Cox proportional hazards model for distribution of OS in each randomized arm. Interim analysis (Primary Endpoint) was planned to occur after at least 196 deaths, with the actual analysis occurring at 199 deaths.

End point type	Primary
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End point timeframe:

Randomization until 199 deaths, up to November 2014, approximately 25 months

End point values	Nivolumab	Docetaxel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	135	137		
Units: months				
median (confidence interval 95%)	9.23 (7.33 to 13.27)	6.01 (5.13 to 7.33)		

Statistical analyses

Statistical analysis title	Overall Survival
Comparison groups	Nivolumab v Docetaxel
Number of subjects included in analysis	272
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0002 ^[3]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.59
Confidence interval	
level	Other: 96.85 %
sides	2-sided
lower limit	0.43
upper limit	0.81

Notes:

[3] - Stratified by region (US/Canada, Rest Of World (ROW), Europe) and prior treatment regimen (Paclitaxel, Another agent) as entered in the Interactive Voice Response System (IVRS).

Secondary: Objective Response Rate (ORR) in All Randomized Participants

End point title	Objective Response Rate (ORR) in All Randomized Participants
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End point description:

ORR was defined as the percentage of all randomized participants whose Best Overall Response (BOR) was a confirmed Complete Response (CR) or Partial Response (PR). BOR was defined as the best investigator-assessed response designation, recorded between the date of randomization and the date of objectively documented progression per Response Evaluation Criteria in Solid Tumors version 1.1 (RECIST v1.1) or the date of subsequent anti-cancer therapy (excluding on-treatment palliative radiotherapy of non-target bone lesions or Central Nervous System (CNS) lesions), whichever occurred first. CR = Disappearance of all target lesions. Any pathological lymph nodes (whether target or non-target) must have reduction in short axis to < 10 mm.; PR = At least a 30% decrease in the sum of diameters of target lesions, taking as reference, the baseline sum diameters. CIs were computed using the Clopper and Pearson method.

End point type	Secondary
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End point timeframe:

From the date of randomization up to the final database lock, up to approximately 108 months

End point values	Nivolumab	Docetaxel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	135	137		
Units: percentage of participants				
number (confidence interval 95%)	20.0 (13.6 to 27.7)	8.8 (4.6 to 14.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Time To Response (TTR) in Months for All Confirmed Responders

End point title	Time To Response (TTR) in Months for All Confirmed Responders
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End point description:

Time to Response (TTR) for participants demonstrating a response (either CR or PR) was defined as the time from the date of randomization to the date of the first confirmed response. CR = Disappearance of all target lesions. Any pathological lymph nodes (whether target or non-target) must have reduction in short axis to < 10 mm.; PR = At least a 30% decrease in the sum of diameters of target lesions, taking, as reference, the baseline sum diameters.

End point type	Secondary
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End point timeframe:

From the date of randomization up to the final database lock, up to approximately 108 months

End point values	Nivolumab	Docetaxel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	27	12		
Units: Months				
median (full range (min-max))	2.23 (1.6 to 11.8)	2.09 (1.8 to 9.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Objective Response (DOR) in Months for All Confirmed Responders

End point title	Duration of Objective Response (DOR) in Months for All Confirmed Responders
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End point description:

DOR was defined as the time from the date of first confirmed response to the date of the first documented tumor progression (per RECIST v1.1), as determined by the investigator, or death due to any cause, whichever occurred first. DOR was evaluated only for confirmed responders (i.e. participants with confirmed CR or PR). CR = Disappearance of all target lesions. Any pathological lymph nodes (whether target or non-target) must have reduction in short axis to < 10 mm.; PR = At least a 30% decrease in the sum of diameters of target lesions, taking, as reference, the baseline sum diameters. Participants who neither progressed nor died were censored on the date of their last evaluable tumor assessment.

End point type	Secondary
End point timeframe:	
From the date of randomization up to the final database lock, up to approximately 108 months	

End point values	Nivolumab	Docetaxel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	27	12		
Units: Months				
median (confidence interval 95%)	24.51 (9.76 to 69.65)	8.41 (3.58 to 14.03)		

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-Free Survival (PFS) Time in Months for All Randomized Participants

End point title	Progression-Free Survival (PFS) Time in Months for All Randomized Participants
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End point description:

PFS was defined as the time from the date of randomization to the date of the first documented tumor progression as determined by the investigator per RECIST v1.1 criteria, or death due to any cause. Participants underwent radiographic tumor assessments every 6 weeks (+/- 5 days) from week 9 (+/- 5 days) for the first year on treatment, then every 12 weeks after the first year on treatment until documented disease progression. Participants who did not progress or die were censored on the date of their last evaluable tumor assessment. Participants who started any subsequent anti-cancer therapy (including on-treatment palliative RT of non-target bone lesions or CNS lesions) without a prior reported progression were to be censored at the last evaluable tumor assessment prior to or on initiation of the subsequent anti-cancer therapy.

End point type	Secondary
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End point timeframe:

From the date of randomization up to the final database lock, up to approximately 108 months

End point values	Nivolumab	Docetaxel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	135	137		
Units: Months				
median (confidence interval 95%)	3.48 (2.14 to 5.06)	2.83 (2.10 to 3.52)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Experiencing Disease-related Symptom Improvement by Week 12

End point title	Percentage of Participants Experiencing Disease-related Symptom Improvement by Week 12
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End point description:

Disease-related symptom improvement rate by Week 12 was defined as the percentage of randomized participants who had a 10 point or greater decrease from baseline in average symptom burden index score at any time between randomization and Week 12. The participant portion of the Lung Cancer Symptom Scale (LCSS) consisted of 6 symptom-specific questions that addressed cough, dyspnea, fatigue, pain, hemoptysis, and anorexia, plus 3 summary items on symptom distress, interference with activity level, and global health-related Quality of Life (QoL). The scores range from 0 to 100, with 0 representing the best possible score and 100 being the worst possible score. The average symptom burden index score at each assessment was defined as the mean of the 6 symptom-specific questions of the LCSS. 95% CIs were computed using Clopper-Pearson Method.

End point type	Secondary
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End point timeframe:

From randomization up to Week 12

End point values	Nivolumab	Docetaxel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	135	137		
Units: percentage of participants				
number (confidence interval 95%)	18.5 (12.4 to 26.1)	21.2 (14.7 to 29.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS) Time in Months by Baseline PD-L1 Expression for All Randomized Participants

End point title	Overall Survival (OS) Time in Months by Baseline PD-L1 Expression for All Randomized Participants
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End point description:

OS was measured in months for all randomized participants grouped by their baseline PD-L1 expression level. PD-L1 expression was defined as the percent of disease tumor cells demonstrating plasma membrane PD-L1 staining of any intensity using an immunohistochemistry (IHC) assay. OS was defined as the time between the date of randomization and the date of death from any cause. Participants were censored at the date they were last known to be alive. Median OS time was calculated using Kaplan-Meier (KM) method.

End point type	Secondary
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End point timeframe:

From the date of randomization to the date of death from any cause, up to approximately 108 months

End point values	Nivolumab	Docetaxel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	135	137		
Units: Months				
median (confidence interval 95%)				
PD-L1 expression \geq 5%	9.95 (5.82 to 16.69)	6.37 (4.50 to 9.03)		
PD-L1 expression $<$ 5%	8.54 (5.49 to 12.62)	6.14 (5.13 to 8.28)		
PD-L1 not quantifiable at baseline	9.41 (7.10 to 25.20)	5.06 (3.02 to 6.11)		

Statistical analyses

No statistical analyses for this end point

Secondary: Objective Response Rate (ORR) by Baseline PD-L1 Expression for All Randomized Participants

End point title	Objective Response Rate (ORR) by Baseline PD-L1 Expression for All Randomized Participants
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End point description:

ORR was reported for all randomized participants grouped by their baseline PD-L1 expression level. ORR was defined as the percentage of all randomized participants whose Best Overall Response (BOR) was a confirmed Complete Response (CR) or Partial Response (PR). PD-L1 expression in participants was defined as the percent of disease tumor cells demonstrating plasma membrane PD-L1 staining of any intensity using an immunohistochemistry (IHC) assay. CR = Disappearance of all target lesions. Any pathological lymph nodes (whether target or non-target) must have reduction in short axis to $<$ 10 mm.; PR = At least a 30% decrease in the sum of diameters of target lesions, taking, as reference, the baseline sum diameters. CIs were computed using the Clopper and Pearson method.

End point type	Secondary
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End point timeframe:

From the date of randomization up to the final database lock, up to approximately 108 months

End point values	Nivolumab	Docetaxel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	135	137		
Units: Percentage of participants				
number (confidence interval 95%)				
PD-L1 expression \geq 5%	21.4 (10.3 to 36.8)	7.7 (1.6 to 20.9)		
PD-L1 expression $<$ 5%	14.7 (7.6 to 24.7)	11.6 (5.1 to 21.6)		
PD-L1 not quantifiable at baseline	38.9 (17.3 to 64.3)	3.4 (0.1 to 17.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Progression Free Survival (PFS) Time in Months by Baseline PD-L1 Expression for All Randomized Participants

End point title	Progression Free Survival (PFS) Time in Months by Baseline PD-L1 Expression for All Randomized Participants
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End point description:

PFS time was measured for all randomized participants grouped by their baseline PD-L1 expression levels. PFS was defined as the time from the date of randomization to the date of the first documented tumor progression as determined by the investigator per RECIST v1.1 criteria, or death due to any cause. The PFS curves were estimated using KM method. Participants who did not progress or die were censored on the date of their last evaluable tumor assessment. Participants who started subsequent anti-cancer therapy (including on-treatment palliative radiotherapy of non-target bone lesions or CNS lesions) without a prior reported progression were censored at the last evaluable tumor assessment prior to subsequent anti-cancer therapy.

End point type	Secondary
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End point timeframe:

From the date of randomization up to the final database lock, up to approximately 108 months

End point values	Nivolumab	Docetaxel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	135	137		
Units: Months				
median (confidence interval 95%)				
PD-L1 expression \geq 5%	5.06 (2.10 to 7.56)	3.06 (1.94 to 4.63)		
PD-L1 expression $<$ 5%	2.23 (1.94 to 4.73)	2.92 (2.07 to 3.58)		
PD-L1 not quantifiable at baseline	5.39 (2.10 to 10.45)	2.23 (2.04 to 4.40)		

Statistical analyses

No statistical analyses for this end point

Secondary: Progression Free Survival Rate (PFSR)

End point title	Progression Free Survival Rate (PFSR)
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End point description:

PFSR was defined as the percentage of participants who did not experience disease progression or death from any cause at a given time point following randomization. Progression was assessed by investigators according to RECIST v1.1. Participants who did not progress or die were censored on the date of their last evaluable tumor assessment. Participants who started any subsequent anti-cancer therapy (including on-treatment palliative radiation therapy (RT) of non-target bone lesions or CNS lesions) without a prior reported progression were to be censored at the last evaluable tumor assessment prior to or on initiation of the subsequent anti-cancer therapy. "999"=N/A

End point type	Secondary
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End point timeframe:

From randomization to specified timepoints, up to 84 months

End point values	Nivolumab	Docetaxel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	135	137		
Units: Percentage of participants				
number (confidence interval 95%)				
6 months	38.4 (30.0 to 46.8)	22.6 (15.7 to 30.2)		
12 months	21.0 (14.3 to 28.6)	7.2 (3.4 to 12.8)		
18 months	15.87 (9.9 to 22.8)	1.8 (0.4 to 5.7)		
24 months	14.8 (9.1 to 21.8)	999 (999 to 999)		
36 months	11.0 (6.1 to 17.5)	999 (999 to 999)		
48 months	8.9 (4.5 to 15.1)	999 (999 to 999)		
60 months	8.9 (4.5 to 15.1)	999 (999 to 999)		
72 months	7.6 (3.5 to 13.7)	999 (999 to 999)		
84 months	6.1 (2.4 to 12.2)	999 (999 to 999)		

Statistical analyses

No statistical analyses for this end point

Post-hoc: Overall Survival (OS) Rate in All Randomized Participants at Study Completion

End point title	Overall Survival (OS) Rate in All Randomized Participants at Study Completion
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End point description:

The overall survival rate is the probability that a participant will be alive at the specified timepoints following randomization. Overall survival was defined as the time between the date of randomization and the date of death as a result of any cause. Survival rates were determined via Kaplan-Meier estimates. "999"=N/A

End point type	Post-hoc
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End point timeframe:

From the date of randomization up to the specified timepoints, up to 84 months

End point values	Nivolumab	Docetaxel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	135	137		
Units: Months				
median (confidence interval 95%)				
6 months	63.7 (55.0 to 71.2)	50.4 (41.7 to 58.4)		
12 months	42.2 (33.8 to 50.4)	24.1 (17.3 to 31.5)		
18 months	28.1 (20.8 to 35.9)	12.4 (7.6 to 18.5)		
24 months	23.0 (16.3 to 30.3)	8.0 (4.3 to 13.3)		
36 months	15.6 (10.0 to 22.2)	5.8 (2.7 to 10.6)		
48 months	13.1 (8.1 to 19.5)	4.4 (1.8 to 8.8)		
60 months	12.3 (7.4 to 18.5)	3.6 (1.4 to 7.8)		
72 months	11.4 (6.7 to 17.5)	2.7 (0.8 to 6.7)		
84 months	9.6 (5.3 to 15.5)	0.0 (-999 to 999)		

Statistical analyses

No statistical analyses for this end point

Post-hoc: Overall Survival (OS) Time in Months for All Randomized Participants at Study Completion

End point title	Overall Survival (OS) Time in Months for All Randomized Participants at Study Completion
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End point description:

OS was defined as the time between the date of randomization and the date of death from any cause. Participants were censored at the date they were last known to be alive. Median OS time was calculated using Kaplan-Meier (KM) method. Hazard ratio (HR) and the corresponding Confidence Interval (CI) were estimated in a stratified Cox proportional hazards model for distribution of OS in each randomized arm. Survival follow-up analysis occurred at the end of the study.

End point type	Post-hoc
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End point timeframe:

From the date of randomization up to the final database lock, up to approximately 108 months

End point values	Nivolumab	Docetaxel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	135	137		
Units: Months				
median (confidence interval 95%)	9.23 (7.33 to 12.62)	6.01 (5.13 to 7.33)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Assessed from date of first dose to 100 days following date of last dose (up to approximately 108 months).

Adverse event reporting additional description:

All-cause mortality, serious adverse events, and adverse events were reported for all treated participants.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
Dictionary version	MedDRA24.0

Reporting groups

Reporting group title	DOCETAXEL
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Reporting group description:

Docetaxel 75mg/m² solution intravenously every 3 weeks until documented disease progression , discontinuation due to toxicity, withdrawal of consent or study ends. Eligible patients may receive nivolumab 3 mg/kg every 2 weeks and/or nivolumab 480 mg flat dose every 4 weeks via extension phase until documented disease progression, discontinuation due to toxicity, withdrawal of consent or study ends.

Reporting group title	NIVOLUMAB
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Reporting group description:

Nivolumab 3 mg/kg solution intravenously every 2 weeks until documented disease progression, discontinuation due to toxicity, withdrawal of consent or the study ends. Eligible patients may receive nivolumab at 480mg every 4 weeks until documented disease progression, discontinuation, withdrawal of consent or the study ends.

Serious adverse events	DOCETAXEL	NIVOLUMAB	
Total subjects affected by serious adverse events			
subjects affected / exposed	93 / 129 (72.09%)	86 / 131 (65.65%)	
number of deaths (all causes)	127	117	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour pain			
subjects affected / exposed	1 / 129 (0.78%)	0 / 131 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malignant neoplasm progression			
subjects affected / exposed	36 / 129 (27.91%)	40 / 131 (30.53%)	
occurrences causally related to treatment / all	0 / 36	0 / 43	
deaths causally related to treatment / all	0 / 33	0 / 36	
Metastases to central nervous system			

subjects affected / exposed	1 / 129 (0.78%)	0 / 131 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Basal cell carcinoma			
subjects affected / exposed	1 / 129 (0.78%)	0 / 131 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric cancer			
subjects affected / exposed	0 / 129 (0.00%)	1 / 131 (0.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung neoplasm malignant			
subjects affected / exposed	0 / 129 (0.00%)	1 / 131 (0.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Squamous cell carcinoma			
subjects affected / exposed	1 / 129 (0.78%)	0 / 131 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Vascular disorders			
Arterial haemorrhage			
subjects affected / exposed	1 / 129 (0.78%)	0 / 131 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral ischaemia			
subjects affected / exposed	0 / 129 (0.00%)	1 / 131 (0.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Superior vena cava syndrome			
subjects affected / exposed	1 / 129 (0.78%)	0 / 131 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Aortic aneurysm rupture			

subjects affected / exposed	0 / 129 (0.00%)	1 / 131 (0.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 129 (0.78%)	5 / 131 (3.82%)	
occurrences causally related to treatment / all	1 / 1	3 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chills			
subjects affected / exposed	0 / 129 (0.00%)	1 / 131 (0.76%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Asthenia			
subjects affected / exposed	2 / 129 (1.55%)	0 / 131 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General physical health deterioration			
subjects affected / exposed	1 / 129 (0.78%)	1 / 131 (0.76%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sudden death			
subjects affected / exposed	1 / 129 (0.78%)	1 / 131 (0.76%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Fatigue			
subjects affected / exposed	1 / 129 (0.78%)	1 / 131 (0.76%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple organ dysfunction syndrome			
subjects affected / exposed	0 / 129 (0.00%)	1 / 131 (0.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Oedema peripheral			

subjects affected / exposed	0 / 129 (0.00%)	1 / 131 (0.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain			
subjects affected / exposed	1 / 129 (0.78%)	0 / 131 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Swelling			
subjects affected / exposed	1 / 129 (0.78%)	0 / 131 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pneumothorax			
subjects affected / exposed	1 / 129 (0.78%)	0 / 131 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oropharyngeal pain			
subjects affected / exposed	1 / 129 (0.78%)	0 / 131 (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 / 129 (3.10%)	4 / 131 (3.05%)	
occurrences causally related to treatment / all	0 / 4	0 / 4	
deaths causally related to treatment / all	0 / 1	0 / 0	
Haemoptysis			
subjects affected / exposed	2 / 129 (1.55%)	1 / 131 (0.76%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Cough			
subjects affected / exposed	0 / 129 (0.00%)	1 / 131 (0.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary haemorrhage			

subjects affected / exposed	4 / 129 (3.10%)	1 / 131 (0.76%)	
occurrences causally related to treatment / all	1 / 4	0 / 1	
deaths causally related to treatment / all	1 / 4	0 / 1	
Pneumonitis			
subjects affected / exposed	0 / 129 (0.00%)	3 / 131 (2.29%)	
occurrences causally related to treatment / all	0 / 0	3 / 3	
deaths causally related to treatment / all	0 / 0	1 / 1	
Acute respiratory failure			
subjects affected / exposed	1 / 129 (0.78%)	0 / 131 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic obstructive pulmonary disease			
subjects affected / exposed	1 / 129 (0.78%)	2 / 131 (1.53%)	
occurrences causally related to treatment / all	0 / 3	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			
subjects affected / exposed	1 / 129 (0.78%)	1 / 131 (0.76%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary thrombosis			
subjects affected / exposed	0 / 129 (0.00%)	1 / 131 (0.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stridor			
subjects affected / exposed	1 / 129 (0.78%)	0 / 131 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Interstitial lung disease			
subjects affected / exposed	1 / 129 (0.78%)	0 / 131 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Respiratory failure			

subjects affected / exposed	5 / 129 (3.88%)	3 / 131 (2.29%)	
occurrences causally related to treatment / all	0 / 5	0 / 3	
deaths causally related to treatment / all	0 / 5	0 / 3	
Pulmonary embolism			
subjects affected / exposed	2 / 129 (1.55%)	3 / 131 (2.29%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 2	0 / 0	
Respiratory distress			
subjects affected / exposed	1 / 129 (0.78%)	0 / 131 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Bronchial obstruction			
subjects affected / exposed	0 / 129 (0.00%)	1 / 131 (0.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Mental status changes			
subjects affected / exposed	1 / 129 (0.78%)	0 / 131 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Delirium			
subjects affected / exposed	1 / 129 (0.78%)	0 / 131 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Confusional state			
subjects affected / exposed	1 / 129 (0.78%)	0 / 131 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
C-reactive protein increased			
subjects affected / exposed	0 / 129 (0.00%)	1 / 131 (0.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood potassium decreased			

subjects affected / exposed	0 / 129 (0.00%)	1 / 131 (0.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Electrocardiogram abnormal			
subjects affected / exposed	1 / 129 (0.78%)	0 / 131 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 129 (0.00%)	1 / 131 (0.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Radiation oesophagitis			
subjects affected / exposed	1 / 129 (0.78%)	0 / 131 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Cardiac tamponade			
subjects affected / exposed	1 / 129 (0.78%)	1 / 131 (0.76%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinus bradycardia			
subjects affected / exposed	0 / 129 (0.00%)	1 / 131 (0.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardio-respiratory arrest			
subjects affected / exposed	2 / 129 (1.55%)	2 / 131 (1.53%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 2	0 / 2	
Atrial thrombosis			
subjects affected / exposed	0 / 129 (0.00%)	1 / 131 (0.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Atrial fibrillation			
subjects affected / exposed	4 / 129 (3.10%)	0 / 131 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial flutter			
subjects affected / exposed	1 / 129 (0.78%)	0 / 131 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure			
subjects affected / exposed	0 / 129 (0.00%)	1 / 131 (0.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			
subjects affected / exposed	1 / 129 (0.78%)	0 / 131 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericardial effusion			
subjects affected / exposed	1 / 129 (0.78%)	1 / 131 (0.76%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Generalised tonic-clonic seizure			
subjects affected / exposed	0 / 129 (0.00%)	1 / 131 (0.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrovascular accident			
subjects affected / exposed	3 / 129 (2.33%)	0 / 131 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 2	0 / 0	
Ischaemic stroke			
subjects affected / exposed	0 / 129 (0.00%)	1 / 131 (0.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aphasia			

subjects affected / exposed	1 / 129 (0.78%)	0 / 131 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Myasthenic syndrome			
subjects affected / exposed	0 / 129 (0.00%)	1 / 131 (0.76%)	
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	1 / 129 (0.78%)	0 / 131 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal cord compression			
subjects affected / exposed	0 / 129 (0.00%)	1 / 131 (0.76%)	
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 / 129 (0.00%)	1 / 131 (0.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Facial paralysis			
subjects affected / exposed	1 / 129 (0.78%)	0 / 131 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Seizure			
subjects affected / exposed	0 / 129 (0.00%)	1 / 131 (0.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	0 / 129 (0.00%)	1 / 131 (0.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			

subjects affected / exposed	0 / 129 (0.00%)	2 / 131 (1.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile neutropenia			
subjects affected / exposed	13 / 129 (10.08%)	0 / 131 (0.00%)	
occurrences causally related to treatment / all	14 / 14	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenia			
subjects affected / exposed	3 / 129 (2.33%)	1 / 131 (0.76%)	
occurrences causally related to treatment / all	3 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile bone marrow aplasia			
subjects affected / exposed	1 / 129 (0.78%)	0 / 131 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancytopenia			
subjects affected / exposed	1 / 129 (0.78%)	0 / 131 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myelosuppression			
subjects affected / exposed	1 / 129 (0.78%)	0 / 131 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			
subjects affected / exposed	1 / 129 (0.78%)	0 / 131 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	3 / 129 (2.33%)	0 / 131 (0.00%)	
occurrences causally related to treatment / all	2 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			

subjects affected / exposed	1 / 129 (0.78%)	0 / 131 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal perforation			
subjects affected / exposed	1 / 129 (0.78%)	0 / 131 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			
subjects affected / exposed	1 / 129 (0.78%)	1 / 131 (0.76%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain			
subjects affected / exposed	3 / 129 (2.33%)	0 / 131 (0.00%)	
occurrences causally related to treatment / all	1 / 3	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Dysphagia			
subjects affected / exposed	0 / 129 (0.00%)	3 / 131 (2.29%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Constipation			
subjects affected / exposed	1 / 129 (0.78%)	0 / 131 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophagitis			
subjects affected / exposed	0 / 129 (0.00%)	1 / 131 (0.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophagitis ulcerative			
subjects affected / exposed	1 / 129 (0.78%)	0 / 131 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis			

subjects affected / exposed	0 / 129 (0.00%)	1 / 131 (0.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumoperitoneum			
subjects affected / exposed	1 / 129 (0.78%)	0 / 131 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Immune-mediated hepatitis			
subjects affected / exposed	0 / 129 (0.00%)	1 / 131 (0.76%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Tubulointerstitial nephritis			
subjects affected / exposed	0 / 129 (0.00%)	1 / 131 (0.76%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematuria			
subjects affected / exposed	0 / 129 (0.00%)	1 / 131 (0.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ureterolithiasis			
subjects affected / exposed	1 / 129 (0.78%)	0 / 131 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	0 / 129 (0.00%)	1 / 131 (0.76%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Goitre			
subjects affected / exposed	1 / 129 (0.78%)	0 / 131 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Adrenal insufficiency			
subjects affected / exposed	1 / 129 (0.78%)	0 / 131 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 129 (0.00%)	1 / 131 (0.76%)	
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	1 / 129 (0.78%)	0 / 131 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neck pain			
subjects affected / exposed	1 / 129 (0.78%)	0 / 131 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Enterocolitis infectious			
subjects affected / exposed	1 / 129 (0.78%)	0 / 131 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infection			
subjects affected / exposed	1 / 129 (0.78%)	0 / 131 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin infection			
subjects affected / exposed	1 / 129 (0.78%)	0 / 131 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	18 / 129 (13.95%)	15 / 131 (11.45%)	
occurrences causally related to treatment / all	3 / 21	0 / 16	
deaths causally related to treatment / all	0 / 2	0 / 3	

Upper respiratory tract infection subjects affected / exposed	0 / 129 (0.00%)	2 / 131 (1.53%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection subjects affected / exposed	0 / 129 (0.00%)	1 / 131 (0.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenic infection subjects affected / exposed	1 / 129 (0.78%)	0 / 131 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis subjects affected / exposed	1 / 129 (0.78%)	2 / 131 (1.53%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic shock subjects affected / exposed	1 / 129 (0.78%)	1 / 131 (0.76%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium difficile colitis subjects affected / exposed	1 / 129 (0.78%)	0 / 131 (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	2 / 129 (1.55%)	1 / 131 (0.76%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Sepsis subjects affected / exposed	4 / 129 (3.10%)	1 / 131 (0.76%)	
occurrences causally related to treatment / all	1 / 4	0 / 1	
deaths causally related to treatment / all	1 / 1	0 / 1	
Respiratory tract infection			

subjects affected / exposed	1 / 129 (0.78%)	1 / 131 (0.76%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacterial infection			
subjects affected / exposed	1 / 129 (0.78%)	0 / 131 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pneumocystis jirovecii pneumonia			
subjects affected / exposed	0 / 129 (0.00%)	1 / 131 (0.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral infection			
subjects affected / exposed	0 / 129 (0.00%)	1 / 131 (0.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	3 / 129 (2.33%)	2 / 131 (1.53%)	
occurrences causally related to treatment / all	2 / 3	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 0	
Hypercalcaemia			
subjects affected / exposed	1 / 129 (0.78%)	4 / 131 (3.05%)	
occurrences causally related to treatment / all	0 / 1	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyponatraemia			
subjects affected / exposed	1 / 129 (0.78%)	0 / 131 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoglycaemia			
subjects affected / exposed	1 / 129 (0.78%)	0 / 131 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypophosphataemia			

subjects affected / exposed	0 / 129 (0.00%)	1 / 131 (0.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Failure to thrive			
subjects affected / exposed	0 / 129 (0.00%)	1 / 131 (0.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Hyperglycaemia			
subjects affected / exposed	0 / 129 (0.00%)	1 / 131 (0.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypokalaemia			
subjects affected / exposed	0 / 129 (0.00%)	1 / 131 (0.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypomagnesaemia			
subjects affected / exposed	0 / 129 (0.00%)	1 / 131 (0.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	DOCETAXEL	NIVOLUMAB	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	122 / 129 (94.57%)	119 / 131 (90.84%)	
Vascular disorders			
Hypotension			
subjects affected / exposed	5 / 129 (3.88%)	7 / 131 (5.34%)	
occurrences (all)	6	7	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	27 / 129 (20.93%)	27 / 131 (20.61%)	
occurrences (all)	33	40	
Chest pain			

subjects affected / exposed	11 / 129 (8.53%)	6 / 131 (4.58%)	
occurrences (all)	11	6	
Chills			
subjects affected / exposed	3 / 129 (2.33%)	9 / 131 (6.87%)	
occurrences (all)	3	11	
Mucosal inflammation			
subjects affected / exposed	13 / 129 (10.08%)	3 / 131 (2.29%)	
occurrences (all)	16	3	
Fatigue			
subjects affected / exposed	52 / 129 (40.31%)	42 / 131 (32.06%)	
occurrences (all)	65	58	
Asthenia			
subjects affected / exposed	27 / 129 (20.93%)	26 / 131 (19.85%)	
occurrences (all)	34	30	
Oedema peripheral			
subjects affected / exposed	16 / 129 (12.40%)	11 / 131 (8.40%)	
occurrences (all)	18	14	
Non-cardiac chest pain			
subjects affected / exposed	2 / 129 (1.55%)	8 / 131 (6.11%)	
occurrences (all)	2	10	
Pain			
subjects affected / exposed	6 / 129 (4.65%)	8 / 131 (6.11%)	
occurrences (all)	7	9	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	39 / 129 (30.23%)	47 / 131 (35.88%)	
occurrences (all)	43	55	
Haemoptysis			
subjects affected / exposed	11 / 129 (8.53%)	9 / 131 (6.87%)	
occurrences (all)	13	11	
Cough			
subjects affected / exposed	26 / 129 (20.16%)	45 / 131 (34.35%)	
occurrences (all)	26	60	
Dysphonia			

subjects affected / exposed occurrences (all)	1 / 129 (0.78%) 1	11 / 131 (8.40%) 11	
Productive cough subjects affected / exposed occurrences (all)	5 / 129 (3.88%) 5	7 / 131 (5.34%) 7	
Psychiatric disorders Insomnia subjects affected / exposed occurrences (all)	7 / 129 (5.43%) 8	9 / 131 (6.87%) 10	
Investigations Neutrophil count decreased subjects affected / exposed occurrences (all)	8 / 129 (6.20%) 8	0 / 131 (0.00%) 0	
Weight decreased subjects affected / exposed occurrences (all)	9 / 129 (6.98%) 11	13 / 131 (9.92%) 14	
White blood cell count decreased subjects affected / exposed occurrences (all)	8 / 129 (6.20%) 9	0 / 131 (0.00%) 0	
Blood alkaline phosphatase increased subjects affected / exposed occurrences (all)	3 / 129 (2.33%) 3	8 / 131 (6.11%) 11	
Nervous system disorders Paraesthesia subjects affected / exposed occurrences (all)	9 / 129 (6.98%) 10	5 / 131 (3.82%) 6	
Headache subjects affected / exposed occurrences (all)	10 / 129 (7.75%) 11	19 / 131 (14.50%) 22	
Dizziness subjects affected / exposed occurrences (all)	13 / 129 (10.08%) 14	13 / 131 (9.92%) 17	
Neuropathy peripheral subjects affected / exposed occurrences (all)	14 / 129 (10.85%) 14	4 / 131 (3.05%) 5	
Blood and lymphatic system disorders			

Anaemia			
subjects affected / exposed	43 / 129 (33.33%)	27 / 131 (20.61%)	
occurrences (all)	55	37	
Leukopenia			
subjects affected / exposed	11 / 129 (8.53%)	3 / 131 (2.29%)	
occurrences (all)	17	5	
Neutropenia			
subjects affected / exposed	43 / 129 (33.33%)	4 / 131 (3.05%)	
occurrences (all)	57	6	
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	20 / 129 (15.50%)	14 / 131 (10.69%)	
occurrences (all)	26	18	
Diarrhoea			
subjects affected / exposed	34 / 129 (26.36%)	24 / 131 (18.32%)	
occurrences (all)	37	42	
Nausea			
subjects affected / exposed	35 / 129 (27.13%)	25 / 131 (19.08%)	
occurrences (all)	43	34	
Abdominal pain			
subjects affected / exposed	10 / 129 (7.75%)	8 / 131 (6.11%)	
occurrences (all)	11	10	
Constipation			
subjects affected / exposed	19 / 129 (14.73%)	18 / 131 (13.74%)	
occurrences (all)	20	18	
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	4 / 129 (3.10%)	11 / 131 (8.40%)	
occurrences (all)	6	11	
Rash			
subjects affected / exposed	12 / 129 (9.30%)	12 / 131 (9.16%)	
occurrences (all)	13	13	
Alopecia			
subjects affected / exposed	30 / 129 (23.26%)	2 / 131 (1.53%)	
occurrences (all)	30	2	
Endocrine disorders			

Hypothyroidism subjects affected / exposed occurrences (all)	0 / 129 (0.00%) 0	7 / 131 (5.34%) 8	
Musculoskeletal and connective tissue disorders			
Bone pain subjects affected / exposed occurrences (all)	7 / 129 (5.43%) 8	3 / 131 (2.29%) 4	
Musculoskeletal chest pain subjects affected / exposed occurrences (all)	4 / 129 (3.10%) 4	7 / 131 (5.34%) 9	
Myalgia subjects affected / exposed occurrences (all)	15 / 129 (11.63%) 21	3 / 131 (2.29%) 4	
Back pain subjects affected / exposed occurrences (all)	12 / 129 (9.30%) 14	14 / 131 (10.69%) 18	
Arthralgia subjects affected / exposed occurrences (all)	19 / 129 (14.73%) 24	17 / 131 (12.98%) 24	
Infections and infestations			
Upper respiratory tract infection subjects affected / exposed occurrences (all)	5 / 129 (3.88%) 5	8 / 131 (6.11%) 12	
Bronchitis subjects affected / exposed occurrences (all)	4 / 129 (3.10%) 4	15 / 131 (11.45%) 18	
Pneumonia subjects affected / exposed occurrences (all)	7 / 129 (5.43%) 7	6 / 131 (4.58%) 6	
Urinary tract infection subjects affected / exposed occurrences (all)	7 / 129 (5.43%) 12	4 / 131 (3.05%) 4	
Metabolism and nutrition disorders			
Hypercalcaemia subjects affected / exposed occurrences (all)	3 / 129 (2.33%) 3	7 / 131 (5.34%) 10	

Hypomagnesaemia subjects affected / exposed occurrences (all)	5 / 129 (3.88%) 5	8 / 131 (6.11%) 9	
Decreased appetite subjects affected / exposed occurrences (all)	43 / 129 (33.33%) 54	35 / 131 (26.72%) 38	
Hyperglycaemia subjects affected / exposed occurrences (all)	10 / 129 (7.75%) 10	9 / 131 (6.87%) 11	
Hypokalaemia subjects affected / exposed occurrences (all)	4 / 129 (3.10%) 5	7 / 131 (5.34%) 8	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
08 March 2013	Updated to include language on contraception and adverse pregnancy outcomes
29 May 2013	Added "CheckMate 017, CHECKpoint pathway and nivolumAb clinical Trial Evaluation" to the protocol title; replaced the BMS number with nivolumab throughout the document; updated table naming convention; 2nd and 4th secondary objectives updated; added clarifying language on premedication for docetaxel; added nephrotoxicity to the safety information; clarified exclusion criteria; updated peripheral blood markers
25 April 2014	Modification to overall survival analysis; modification to move objective response rate from co-primary endpoint to secondary endpoint
26 January 2015	Added provision for eligible subjects randomized to docetaxel arm to receive subsequent nivolumab treatment as part of a nivolumab extension phase; modifications to the Time and Events Schedule
15 September 2016	Added option for the nivolumab treatment group to switch to a flat dose of nivolumab at 480mg every 4 weeks; updated to allow 30 minute nivolumab infusions; updated contraception requirements

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported