Clinical trial results:
An Open-label, Single-arm Phase II Safety Study of Nivolumab in Participants with Advanced or Metastatic Non-small Cell Lung Cancer Who Have Progressed During or After Receiving at Least One Prior Systemic Regimen

Summary

EudraCT number	2016-003731-37
Trial protocol	RO
Global end of trial date	14 March 2022

Results information

Result version number	v1 (current)
This version publication date	15 December 2022
First version publication date	15 December 2022

Trial information

Trial identification

Sponsor protocol code	CA209-907

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	20 May 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	14 March 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The safety profile of less frequent dosing regimen of 480 mg of nivolumab every 4 weeks is expected to be similar to that of 3 mg/kg of nivolumab every 2 weeks in participants with advanced or metastatic NSCLC. The analyses to summarize incidence of treatment-related select adverse events will be descriptive.

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	16 January 2017
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	1 Years
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Canada: 24
Country: Number of subjects enrolled	Japan: 20
Country: Number of subjects enrolled	Romania: 65
Country: Number of subjects enrolled	South Africa: 16
Country: Number of subjects enrolled	United States: 4
Worldwide total number of subjects	129
EEA total number of subjects	65

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	0

months)	
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	74
From 65 to 84 years	55
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

129 participants were treated

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Arm title	Nivolumab 480mg Q4W

Arm description:

480 mg of Nivolumab every 4 weeks (Q4W) until progression, unacceptable toxicity, withdrawal of consent, death, or a max of 2 years, whichever occurs first

Arm type	Experimental
Investigational medicinal product name	Nivolumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Nivolumab 480 mg every 4 weeks

Number of subjects in period 1	Nivolumab 480mg Q4W
Started	129
Completed	0
Not completed	129
Disease progression	98
Study drug toxicity	4
Maximum clinical benefit	2
Adverse event unrelated to study drug	7
Other reasons	1
Completed treatment as per protocol	17

Baseline characteristics

Reporting groups	
Reporting group title	Nivolumab 480mg Q4W
Reporting group description:	
480 mg of Nivolumab every 4 weeks (Q4W) until progression, unacceptable toxicity, withdrawal of consent, death, or a max of 2 years, whichever occurs first	

Reporting group values	Nivolumab 480mg Q4W	Total	
Number of subjects	129	129	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	74	74	
From 65-84 years	55	55	
85 years and over	0	0	
Age Continuous Units: Years			
arithmetic mean	61.8		
standard deviation	± 10.2	-	
Sex: Female, Male Units:			
Female	34	34	
Male	95	95	
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	26	26	
Native Hawaiian or Other Pacific Islander	0	0	
Black or African American	3	3	
White	95	95	
More than one race	0	0	
Unknown or Not Reported	5	5	
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	1	1	
Not Hispanic or Latino	41	41	
Unknown or Not Reported	87	87	

End points

End points reporting groups

Reporting group title	Nivolumab 480mg Q4W

Reporting group description:

480 mg of Nivolumab every 4 weeks (Q4W) until progression, unacceptable toxicity, withdrawal of consent, death, or a max of 2 years, whichever occurs first

Primary: The number of participants experiencing high grade (Grades 3-4 and Grade 5) Drug-Related Select Adverse Events (AE)

End point title	The number of participants experiencing high grade (Grades 3-4 and Grade 5) Drug-Related Select Adverse Events (AE)[1]

End point description:

The number of participants who experienced at least 1 select AE of Grade 3-5, judged to be related to study drug per investigator with onset on or after first dose of study treatment and within 30 days of last dose of study treatment, divided by number of treated participants. AE grade is defined using National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE) v4.0 criteria. The select AEs consist of pulmonary events, gastrointestinal events, hepatic events, renal events, skin events, endocrine events categories, thyroid disorders, diabetes, pituitary, adrenal disorder subcategories. Grade 3 is defined as severe or medically significant but not immediately life-threatening. Grade 4 is defined as life-threatening consequences and urgent intervention indicated. Grade 5 is defined as death related to AE.

End point type	Primary

End point timeframe:

From the first dose of study treatment to up to 30 days of the last dose of study treatment (up to 24 months)

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: Summary statistics only were planned for this endpoint.

End point values	Nivolumab 480mg Q4W			
Subject group type	Reporting group			
Number of subjects analysed	129			
Units: Participants				
Total Participants with Grade 3-4 AE	3			
Total Participants with Grade 5 AE	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Progression Free Survival (PFS)

End point title	Progression Free Survival (PFS)

End point description:

Progression free survival (PFS) is defined as the time between the date of randomization and the date of the first documented tumor progression accounting for subsequent therapy, based on BICR (blinded independent central review) assessments (per RECIST v1.1 criteria), or death due to any cause, whichever occurs first. Participants will be censored at the last evaluable tumor assessment on or prior to the date of subsequent therapy. 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 mm. (Note: the appearance of one or more new lesions is also considered progression).

End point type	Secondary

End point timeframe:

From first dose to the date of the first documented tumor progression (up to approximately 5 months)

End point values	Nivolumab 480mg Q4W			
Subject group type	Reporting group			
Number of subjects analysed	129			
Units: Months				
median (confidence interval 95%)	3.68 (3.06 to 4.50)			

Statistical analyses

No statistical analyses for this end point

Secondary: Objective Response Rate (ORR)

End point title	Objective Response Rate (ORR)

End point description:

Objective Response Rate (ORR) defined as the percentage of participants with a best overall response (BOR) of confirmed complete response (CR) or partial response (PR) as assessed by investigator per RECIST 1.1. Complete response is defined as the disappearance of all target lesions and the reduction of any pathological lymph nodes to <10 mm. Partial response is defined as at least a 30% decrease in the sum of diameters of target lesions. Radiographic tumor assessments will be conducted at Week 8 (+/- 7 days) and every 8 weeks (+/- 7 days) until up to 2 years or until disease progression (or until discontinuation of study therapy in patients receiving nivolumab beyond progression), lost to follow-up, or withdrawal of study consent.

End point type	Secondary

End point timeframe:

From the date of first dose to the date of the initial objectively documented tumor progression or the date of subsequent therapy, whichever occurs first (up to approximately 25 months).

End point values	Nivolumab 480mg Q4W			
Subject group type	Reporting group			
Number of subjects analysed	129			
Units: Percentage of participants				
number (confidence interval 95%)	17.1 (11.0 to 24.7)			

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS)

End point title	Overall Survival (OS)

End point description:

Overall Survival (OS) is defined as the time between the first dosing date and the date of death due to any cause. For participants without documentation of death, OS will be censored on the last date the participant was known to be alive.

End point type	Secondary

End point timeframe:

From first dosing date and the date of death due to any cause (up to approximately 5 years)

End point values	Nivolumab 480mg Q4W			
Subject group type	Reporting group			
Number of subjects analysed	129			
Units: Months				
median (confidence interval 95%)	10.58 (8.34 to 14.69)			

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (DOR)

End point title	Duration of Response (DOR)

End point description:

Duration of Response (DOR) is defined as the time between the date of first confirmed response up to the date of the first documented tumor progression (per RECIST 1.1) as determined by complete response (CR) or partial response (PR), or death due to any cause, whichever occurs first. Participants who neither progress nor die will be censored on the date of their last evaluable tumor assessment. Participants who started any subsequent anti-cancer therapy (including palliative local therapy) without a prior reported progression will be censored at the last evaluable tumor assessment prior to or on the date of initiation of the subsequent anti-cancer therapy (including palliative local therapy). Complete response is defined as the disappearance of all target lesions and the reduction of any pathological lymph nodes to <10 mm. Partial response is defined as at least a 30% decrease in the sum of diameters of target lesions.

End point type	Secondary

End point timeframe:

From the date of first confirmed response up to the date of the first documented tumor progression (per RECIST 1.1), or death due to any cause, whichever occurs first (up to approximately 48 months).

End point values	Nivolumab 480mg Q4W			
Subject group type	Reporting group			
Number of subjects analysed	22			
Units: Months				
median (confidence interval 95%)	35.45 (10.87 to 47.31)			

Statistical analyses

No statistical analyses for this end point

Post-hoc: The number of participants experiencing high grade (Grades 3-4 and Grade 5) Drug-Related Select Adverse Events (AE) - Extended Collection

End point title	The number of participants experiencing high grade (Grades 3-4 and Grade 5) Drug-Related Select Adverse Events (AE) - Extended Collection

End point description:

The number of participants who experienced at least 1 select AE of Grade 3-5, judged to be related to study drug per investigator with onset on or after first dose of study treatment and within 30 days of last dose of study treatment, divided by number of treated participants. AE grade is defined using National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE) v4.0 criteria. The select AEs consist of pulmonary events, gastrointestinal events, hepatic events, renal events, skin events, endocrine events categories, thyroid disorders, diabetes, pituitary, adrenal disorder subcategories. Grade 3 is defined as severe or medically significant but not immediately life-threatening. Grade 4 is defined as life-threatening consequences and urgent intervention indicated. Grade 5 is defined as death related to AE. Note: This outcome measure represents an update to the primary endpoint to include additional data collection that occurred after the primary completion date.

End point type	Post-hoc

End point timeframe:

From the first dose of study treatment to up to 30 days of the last dose of study treatment (up to 25 months)

End point values	Nivolumab 480mg Q4W			
Subject group type	Reporting group			
Number of subjects analysed	129			
Units: Participants				
Total Participants with Grade 3-4 AE	6			
Total Participants with Grade 5 AE	0			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Participants were assessed for all-cause mortality from their enrollment to study completion, (up to approximately 5 years). SAEs and NAEs were assessed from first dose to 100 days following last dose (up to approximately 27 months)

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25.0

Reporting groups

Reporting group title	Nivolumab 480mg Q4W

Reporting group description:

480 mg of Nivolumab every 4 weeks (Q4W) until progression, unacceptable toxicity, withdrawal of consent, death, or a max of 2 years, whichever occurs first

Serious adverse events	Nivolumab 480mg Q4W		
Total subjects affected by serious adverse events			
subjects affected / exposed	56 / 129 (43.41%)		
number of deaths (all causes)	105		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Lymphangiosis carcinomatosa			
subjects affected / exposed	1 / 129 (0.78%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Malignant neoplasm progression			
subjects affected / exposed	37 / 129 (28.68%)		
occurrences causally related to treatment / all	0 / 37		
deaths causally related to treatment / all	0 / 34		
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	1 / 129 (0.78%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Haemorrhage			

subjects affected / exposed	1 / 129 (0.78%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
General disorders and administration site conditions			
Non-cardiac chest pain			
subjects affected / exposed	1 / 129 (0.78%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General physical health deterioration			
subjects affected / exposed	1 / 129 (0.78%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Acute respiratory distress syndrome			
subjects affected / exposed	1 / 129 (0.78%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Acute respiratory failure			
subjects affected / exposed	1 / 129 (0.78%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Dyspnoea			
subjects affected / exposed	1 / 129 (0.78%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pleural effusion			
subjects affected / exposed	1 / 129 (0.78%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Pneumonitis			
subjects affected / exposed	1 / 129 (0.78%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

Pneumothorax			
subjects affected / exposed	2 / 129 (1.55%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Pulmonary embolism			
subjects affected / exposed	1 / 129 (0.78%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Investigations			
Influenza A virus test positive			
subjects affected / exposed	1 / 129 (0.78%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Injury, poisoning and procedural complications			
Tendon rupture			
subjects affected / exposed	1 / 129 (0.78%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Spinal compression fracture			
subjects affected / exposed	1 / 129 (0.78%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Femoral neck fracture			
subjects affected / exposed	1 / 129 (0.78%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Cardiac tamponade			
subjects affected / exposed	1 / 129 (0.78%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Amnesia			

subjects affected / exposed	1 / 129 (0.78%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Pancytopenia			
subjects affected / exposed	1 / 129 (0.78%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Anaemia			
subjects affected / exposed	1 / 129 (0.78%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	1 / 129 (0.78%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Colitis			
subjects affected / exposed	1 / 129 (0.78%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Vomiting			
subjects affected / exposed	1 / 129 (0.78%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Oesophageal ulcer			
subjects affected / exposed	1 / 129 (0.78%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	1 / 129 (0.78%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		

Cholecystitis chronic			
subjects affected / exposed	1 / 129 (0.78%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Renal impairment			
subjects affected / exposed	1 / 129 (0.78%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Nephrolithiasis			
subjects affected / exposed	1 / 129 (0.78%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Acute kidney injury			
subjects affected / exposed	1 / 129 (0.78%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Bone pain			
subjects affected / exposed	1 / 129 (0.78%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Empyema			
subjects affected / exposed	1 / 129 (0.78%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Diverticulitis			
subjects affected / exposed	1 / 129 (0.78%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastroenteritis			

subjects affected / exposed	1 / 129 (0.78%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Influenza				
subjects affected / exposed	1 / 129 (0.78%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Lower respiratory tract infection				
subjects affected / exposed	1 / 129 (0.78%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Orchitis				
subjects affected / exposed	1 / 129 (0.78%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia				
subjects affected / exposed	6 / 129 (4.65%)			
occurrences causally related to treatment / all	0 / 6			
deaths causally related to treatment / all	0 / 0			
Pneumonia klebsiella				
subjects affected / exposed	1 / 129 (0.78%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia aspiration				
subjects affected / exposed	1 / 129 (0.78%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pulmonary tuberculosis				
subjects affected / exposed	1 / 129 (0.78%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Sepsis				

subjects affected / exposed	1 / 129 (0.78%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection bacterial			
subjects affected / exposed	1 / 129 (0.78%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Hypomagnesaemia			
subjects affected / exposed	1 / 129 (0.78%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hyperglycaemia			
subjects affected / exposed	1 / 129 (0.78%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Nivolumab 480mg Q4W		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	111 / 129 (86.05%)		
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	12 / 129 (9.30%)		
occurrences (all)	18		
Blood alkaline phosphatase increased			
subjects affected / exposed	32 / 129 (24.81%)		
occurrences (all)	38		
Aspartate aminotransferase increased			
subjects affected / exposed	11 / 129 (8.53%)		
occurrences (all)	12		
Blood creatinine increased			

subjects affected / exposed	11 / 129 (8.53%)		
occurrences (all)	15		
Weight decreased			
subjects affected / exposed	14 / 129 (10.85%)		
occurrences (all)	14		
Nervous system disorders			
Dizziness			
subjects affected / exposed	7 / 129 (5.43%)		
occurrences (all)	7		
Headache			
subjects affected / exposed	17 / 129 (13.18%)		
occurrences (all)	17		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	37 / 129 (28.68%)		
occurrences (all)	44		
General disorders and administration site conditions			
Oedema peripheral			
subjects affected / exposed	8 / 129 (6.20%)		
occurrences (all)	8		
Non-cardiac chest pain			
subjects affected / exposed	10 / 129 (7.75%)		
occurrences (all)	10		
Fatigue			
subjects affected / exposed	19 / 129 (14.73%)		
occurrences (all)	20		
Asthenia			
subjects affected / exposed	8 / 129 (6.20%)		
occurrences (all)	8		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	24 / 129 (18.60%)		
occurrences (all)	56		
Constipation			
subjects affected / exposed	9 / 129 (6.98%)		
occurrences (all)	9		

Nausea			
subjects affected / exposed	22 / 129 (17.05%)		
occurrences (all)	28		
Vomiting			
subjects affected / exposed	12 / 129 (9.30%)		
occurrences (all)	14		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	16 / 129 (12.40%)		
occurrences (all)	19		
Dyspnoea			
subjects affected / exposed	23 / 129 (17.83%)		
occurrences (all)	25		
Skin and subcutaneous tissue disorders			
Erythema			
subjects affected / exposed	9 / 129 (6.98%)		
occurrences (all)	9		
Dry skin			
subjects affected / exposed	7 / 129 (5.43%)		
occurrences (all)	8		
Rash			
subjects affected / exposed	26 / 129 (20.16%)		
occurrences (all)	38		
Pruritus			
subjects affected / exposed	24 / 129 (18.60%)		
occurrences (all)	35		
Psychiatric disorders			
Anxiety			
subjects affected / exposed	7 / 129 (5.43%)		
occurrences (all)	7		
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	8 / 129 (6.20%)		
occurrences (all)	8		
Hyperthyroidism			

subjects affected / exposed	7 / 129 (5.43%)		
occurrences (all)	7		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	10 / 129 (7.75%)		
occurrences (all)	12		
Infections and infestations			
Pneumonia			
subjects affected / exposed	13 / 129 (10.08%)		
occurrences (all)	18		
Upper respiratory tract infection			
subjects affected / exposed	7 / 129 (5.43%)		
occurrences (all)	12		
Metabolism and nutrition disorders			
Hypomagnesaemia			
subjects affected / exposed	10 / 129 (7.75%)		
occurrences (all)	11		
Hypoalbuminaemia			
subjects affected / exposed	15 / 129 (11.63%)		
occurrences (all)	18		
Hyperglycaemia			
subjects affected / exposed	13 / 129 (10.08%)		
occurrences (all)	15		
Decreased appetite			
subjects affected / exposed	21 / 129 (16.28%)		
occurrences (all)	23		
Hyponatraemia			
subjects affected / exposed	14 / 129 (10.85%)		
occurrences (all)	17		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
26 January 2018	Increased number of participants in study and sample size determination in statistical section; Updated biomarker section; Allowed participants with known PD-L1 result to receive treatment before submitting tissue; Added requirement of Additional Research for all US sites; Included additional language for nivolumab program level updates; Added the IND Number to Protocol Title Page; Updated information for Study Director and Medical Monitor
10 July 2020	Extended follow-up radiographic tumor assessment collection and survival follow-up to a maximum duration of 5 years after first dose; Updated to bring in line with current nivolumab and BMS protocol standards; Study personnel information updated.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported