Clinical trial results:
A Single-Arm Phase 2 Study of BMS-936558 in Subjects with Advanced or Metastatic Squamous Cell Non-Small Cell Lung Cancer Who Have Received At Least Two Prior Systemic Regimens

Summary

EudraCT number	2012-003965-16
Trial protocol	DE IT FR
Global end of trial date	22 April 2021

Results information

Result version number	v1 (current)
This version publication date	30 April 2022
First version publication date	30 April 2022

Trial information

Trial identification

Sponsor protocol code	CA209-063

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	04 June 2021
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	22 April 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the clinical activity of nivolumab, as measured by the independent radiology review committee (IRC)-assessed objective response rate (ORR), in subjects with advanced or metastatic squamous cell NSCLC who have progressed during or after both platinum doubletbased chemotherapy and at least one additional systemic therapy

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 subjects were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	14 November 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	France: 36
Country: Number of subjects enrolled	Germany: 5
Country: Number of subjects enrolled	Italy: 9
Country: Number of subjects enrolled	United States: 67
Worldwide total number of subjects	117
EEA total number of subjects	50

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)	58
From 65 to 84 years	58
85 years and over	1

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

117 participants treated.

Period 1

Period 1 title	Treatment Period (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Nivolumab, 3 mg/kg

Arm description:

Participants received nivolumab, 3 mg/kg, intravenously over 60 minutes every 2 weeks (on Day 1 of each cycle) until disease progression, discontinuation due to toxicity, withdrawal of consent, or end of study. Every 2-week treatment period was considered to be a cycle.

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

Dosage and administration details:

3 mg/kg every 2 weeks

Number of subjects in period 1	Nivolumab, 3 mg/kg
Started	117
Completed	0
Not completed	117
Adverse Event unrelated to study drug	11
Other Reasons	3
Subject request to discontinue study treatment	3
Death	1
Study Drug Toxcisity	14
Disease Progression	85

Baseline characteristics

Reporting groups	
Reporting group title	Nivolumab, 3 mg/kg
Reporting group description:	
Participants received nivolumab, 3 mg/kg, intravenously over 60 minutes every 2 weeks (on Day 1 of each cycle) until disease progression, discontinuation due to toxicity, withdrawal of consent, or end of study. Every 2-week treatment period was considered to be a cycle.	

Reporting group values	Nivolumab, 3 mg/kg	Total	
Number of subjects	117	117	
Age Categorical Units:			
Younger than 65 years	58	58	
At least 65 years and younger than 75 years	43	43	
75 years and older	16	16	
Age Continuous Units: Years			
arithmetic mean	64.1		
standard deviation	± 9.11	-	
Sex: Female, Male Units:			
Female	32	32	
Male	85	85	
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	0	0	
Not Hispanic or Latino	69	69	
Unknown or Not Reported	48	48	
Race/Ethnicity, Customized Units: Subjects			
White	99	99	
Black or African American	11	11	
American Indian or Alaska Native	0	0	
Asian	2	2	
Native Hawaiian or other Pacific Islander	0	0	
Other	5	5	

End points

End points reporting groups

Reporting group title	Nivolumab, 3 mg/kg

Reporting group description:

Participants received nivolumab, 3 mg/kg, intravenously over 60 minutes every 2 weeks (on Day 1 of each cycle) until disease progression, discontinuation due to toxicity, withdrawal of consent, or end of study. Every 2-week treatment period was considered to be a cycle.

Primary: Objective Response Rate (ORR) as Assessed by Independent Radiology Review Committee (IRC)

End point title	Objective Response Rate (ORR) as Assessed by Independent Radiology Review Committee (IRC)[1]

End point description:

ORR is defined as the percentage of treated participants with confirmed complete response (CR) or partial response (PR) per RECIST 1.1 based on IRC assessment.
The IRC-assessed ORR (using RECIST 1.1 criteria with requirement for response confirmation, and based on the IRC global radiology review after incorporation of on-study clinical data) is summarized by a binomial response rate and its corresponding two-sided 95% exact CIs using Clopper-Pearson method.

End point type	Primary

End point timeframe:

Day 1 of treatment up to approximately 21 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: Statistical Analysis for this Endpoint was not done

End point values	Nivolumab, 3 mg/kg			
Subject group type	Reporting group			
Number of subjects analysed	117			
Units: Percentage of Participants				
number (confidence interval 95%)	14.5 (8.7 to 22.2)			

Statistical analyses

No statistical analyses for this end point

Primary: Duration of Response (DOR) as Assessed by Independent Radiology Review Committee (IRC)

End point title	Duration of Response (DOR) as Assessed by Independent Radiology Review Committee (IRC)[2]

End point description:

DOR is defined as the time from first confirmed response (CR or PR) per IRC assessment to the date of the first documented tumor progression as determined using RECIST 1.1 criteria or death due to any cause, whichever occurs first. Participants who start subsequent therapy without a prior reported progression will be censored at the last evaluable tumor assessments prior to initiation of the subsequent anticancer therapy. Participants who die without a reported prior progression will be considered to have progressed on the date of their death. Participants who neither progress nor die will be censored on the date of their last evaluable tumor assessment. Median values of DOR, along with

two-sided 95% CI in each treatment group will be computed based on a log-log transformation method. Here '9999' signifies data not available

End point type	Primary

End point timeframe:

Day 1 of treatment up to approximately 21 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: Statistical Analysis for this Endpoint was not done

End point values	Nivolumab, 3 mg/kg			
Subject group type	Reporting group			
Number of subjects analysed	17			
Units: Months				
median (confidence interval 95%)	9999 (8.31 to 9999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Objective Response Rate (ORR) as Assessed by Investigator

End point title	Objective Response Rate (ORR) as Assessed by Investigator

End point description:

ORR is defined as the percentage of treated participants with confirmed complete response (CR) or partial response (PR) per RECIST 1.1 based on investigator assessment.
The investigator-assessed ORR is summarized by a binomial response rate and its corresponding two-sided 95% exact CIs using Clopper-Pearson method.

End point type	Secondary

End point timeframe:

Day 1 of treatment to approximately 103 months

End point values	Nivolumab, 3 mg/kg			
Subject group type	Reporting group			
Number of subjects analysed	117			
Units: Percentage of Participants				
number (confidence interval 95%)	15.4 (9.4 to 23.2)			

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (DOR) as Assessed by Investigator

End point title	Duration of Response (DOR) as Assessed by Investigator

End point description:

DOR is defined as the time from first confirmed response (CR or PR) per investigator assessment to the date of the first documented tumor progression as determined using RECIST 1.1 criteria or death due to any cause, whichever occurs first. Participants who start subsequent therapy without a prior reported progression will be censored at the last evaluable tumor assessments prior to initiation of the subsequent anticancer therapy. Participants who die without a reported prior progression will be considered to have progressed on the date of their death. Participants who neither progress nor die will be censored on the date of their last evaluable tumor assessment. Median values of DOR, along with two-sided 95% CI in each treatment group will be computed based on a log-log transformation method.

End point type	Secondary

End point timeframe:

From the first confirmed response to the date of the first documented tumor progression or death. Approximately up to 103 months

End point values	Nivolumab, 3 mg/kg			
Subject group type	Reporting group			
Number of subjects analysed	18			
Units: Months				
median (confidence interval 95%)	16.00 (12.45 to 29.54)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From the first visit to 100 days after last treatment. Approximately up to 103 months	
Adverse event reporting additional description:	
101 deaths occurred on or before the last disposition date; 7 deaths occurred after the last disposition date	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	MedDRA 24

Reporting groups	
Reporting group title	Nivolumab, 3 mg/kg
Reporting group description:	
Participants received nivolumab, 3 mg/kg, intravenously over 60 minutes every 2 weeks (on Day 1 of each cycle) until disease progression, discontinuation due to toxicity, withdrawal of consent, or end of study. Every 2-week treatment period was considered to be a cycle.	

Serious adverse events	Nivolumab, 3 mg/kg		
Total subjects affected by serious adverse events			
subjects affected / exposed	88 / 117 (75.21%)		
number of deaths (all causes)	108		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour pain			
subjects affected / exposed	1 / 117 (0.85%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Skin cancer			
subjects affected / exposed	1 / 117 (0.85%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Malignant neoplasm progression			
subjects affected / exposed	33 / 117 (28.21%)		
occurrences causally related to treatment / all	0 / 34		
deaths causally related to treatment / all	0 / 31		
Meningioma			

subjects affected / exposed	1 / 117 (0.85%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Neoplasm progression			
subjects affected / exposed	1 / 117 (0.85%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Superior vena cava syndrome			
subjects affected / exposed	2 / 117 (1.71%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 1		
Aortic aneurysm rupture			
subjects affected / exposed	1 / 117 (0.85%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Embolism			
subjects affected / exposed	1 / 117 (0.85%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Deep vein thrombosis			
subjects affected / exposed	1 / 117 (0.85%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hypotension			
subjects affected / exposed	2 / 117 (1.71%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Pain			
subjects affected / exposed	3 / 117 (2.56%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 1		

Performance status decreased				
subjects affected / exposed	1 / 117 (0.85%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Pyrexia				
subjects affected / exposed	2 / 117 (1.71%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Chest pain				
subjects affected / exposed	1 / 117 (0.85%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Sudden death				
subjects affected / exposed	1 / 117 (0.85%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Immune system disorders				
Anaphylactic reaction				
subjects affected / exposed	1 / 117 (0.85%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Hypersensitivity				
subjects affected / exposed	1 / 117 (0.85%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Dyspnoea				
subjects affected / exposed	10 / 117 (8.55%)			
occurrences causally related to treatment / all	0 / 10			
deaths causally related to treatment / all	0 / 1			
Laryngeal haemorrhage				
subjects affected / exposed	1 / 117 (0.85%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

Pulmonary haemorrhage			
subjects affected / exposed	2 / 117 (1.71%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Pulmonary embolism			
subjects affected / exposed	2 / 117 (1.71%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Pleural effusion			
subjects affected / exposed	4 / 117 (3.42%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Bronchospasm			
subjects affected / exposed	1 / 117 (0.85%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 1		
Acute respiratory failure			
subjects affected / exposed	1 / 117 (0.85%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Chronic obstructive pulmonary disease			
subjects affected / exposed	6 / 117 (5.13%)		
occurrences causally related to treatment / all	0 / 9		
deaths causally related to treatment / all	0 / 1		
Pneumonitis			
subjects affected / exposed	6 / 117 (5.13%)		
occurrences causally related to treatment / all	7 / 7		
deaths causally related to treatment / all	0 / 0		
Haemoptysis			
subjects affected / exposed	4 / 117 (3.42%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Tachypnoea			

subjects affected / exposed	1 / 117 (0.85%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hypoxia			
subjects affected / exposed	2 / 117 (1.71%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Pneumonia aspiration			
subjects affected / exposed	2 / 117 (1.71%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Pneumothorax			
subjects affected / exposed	1 / 117 (0.85%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory failure			
subjects affected / exposed	3 / 117 (2.56%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 2		
Psychiatric disorders			
Confusional state			
subjects affected / exposed	2 / 117 (1.71%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Investigations			
C-reactive protein increased			
subjects affected / exposed	1 / 117 (0.85%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Spinal fracture			
subjects affected / exposed	1 / 117 (0.85%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Toxicity to various agents				
subjects affected / exposed	1 / 117 (0.85%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Cardiac disorders				
Cardio-respiratory arrest				
subjects affected / exposed	1 / 117 (0.85%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Atrial fibrillation				
subjects affected / exposed	1 / 117 (0.85%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Myocardial infarction				
subjects affected / exposed	1 / 117 (0.85%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Cardiac tamponade				
subjects affected / exposed	1 / 117 (0.85%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pericarditis				
subjects affected / exposed	1 / 117 (0.85%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Supraventricular tachycardia				
subjects affected / exposed	1 / 117 (0.85%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Ventricular tachycardia				
subjects affected / exposed	1 / 117 (0.85%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				

Motor dysfunction			
subjects affected / exposed	1 / 117 (0.85%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Peripheral nerve paresis			
subjects affected / exposed	1 / 117 (0.85%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	1 / 1		
Cognitive disorder			
subjects affected / exposed	2 / 117 (1.71%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Headache			
subjects affected / exposed	1 / 117 (0.85%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Brain oedema			
subjects affected / exposed	1 / 117 (0.85%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Haemorrhage intracranial			
subjects affected / exposed	1 / 117 (0.85%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Haemorrhagic stroke			
subjects affected / exposed	1 / 117 (0.85%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Syncope			
subjects affected / exposed	2 / 117 (1.71%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Seizure			

subjects affected / exposed	1 / 117 (0.85%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Ischaemic stroke				
subjects affected / exposed	1 / 117 (0.85%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	1 / 1			
Gastrointestinal disorders				
Abdominal pain				
subjects affected / exposed	3 / 117 (2.56%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal haemorrhage				
subjects affected / exposed	1 / 117 (0.85%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Dysphagia				
subjects affected / exposed	2 / 117 (1.71%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Large intestinal ulcer				
subjects affected / exposed	1 / 117 (0.85%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Vomiting				
subjects affected / exposed	1 / 117 (0.85%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Diarrhoea				
subjects affected / exposed	2 / 117 (1.71%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Haematemesis				

subjects affected / exposed	1 / 117 (0.85%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Intestinal perforation				
subjects affected / exposed	1 / 117 (0.85%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Renal and urinary disorders				
Acute kidney injury				
subjects affected / exposed	1 / 117 (0.85%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Urinary tract disorder				
subjects affected / exposed	1 / 117 (0.85%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Endocrine disorders				
Adrenal insufficiency				
subjects affected / exposed	1 / 117 (0.85%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal and connective tissue disorders				
Musculoskeletal chest pain				
subjects affected / exposed	2 / 117 (1.71%)			
occurrences causally related to treatment / all	0 / 5			
deaths causally related to treatment / all	0 / 0			
Pathological fracture				
subjects affected / exposed	1 / 117 (0.85%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Arthralgia				
subjects affected / exposed	1 / 117 (0.85%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

Muscular weakness				
subjects affected / exposed	1 / 117 (0.85%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pain in extremity				
subjects affected / exposed	1 / 117 (0.85%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Diverticulitis				
subjects affected / exposed	1 / 117 (0.85%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Wound infection				
subjects affected / exposed	1 / 117 (0.85%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Cellulitis				
subjects affected / exposed	1 / 117 (0.85%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Bronchitis				
subjects affected / exposed	1 / 117 (0.85%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Septic shock				
subjects affected / exposed	2 / 117 (1.71%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 2			
Pulmonary sepsis				
subjects affected / exposed	1 / 117 (0.85%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Herpes zoster				

subjects affected / exposed	1 / 117 (0.85%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia				
subjects affected / exposed	10 / 117 (8.55%)			
occurrences causally related to treatment / all	2 / 11			
deaths causally related to treatment / all	1 / 2			
Meningitis				
subjects affected / exposed	1 / 117 (0.85%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Sepsis				
subjects affected / exposed	1 / 117 (0.85%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Metabolism and nutrition disorders				
Hypercalcaemia				
subjects affected / exposed	6 / 117 (5.13%)			
occurrences causally related to treatment / all	0 / 7			
deaths causally related to treatment / all	0 / 0			
Decreased appetite				
subjects affected / exposed	1 / 117 (0.85%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hyponatraemia				
subjects affected / exposed	1 / 117 (0.85%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Failure to thrive				
subjects affected / exposed	1 / 117 (0.85%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Dehydration				

subjects affected / exposed	1 / 117 (0.85%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Nivolumab, 3 mg/kg		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	110 / 117 (94.02%)		
Vascular disorders			
Hypertension			
subjects affected / exposed	8 / 117 (6.84%)		
occurrences (all)	12		
Hypotension			
subjects affected / exposed	9 / 117 (7.69%)		
occurrences (all)	10		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	62 / 117 (52.99%)		
occurrences (all)	83		
Mucosal inflammation			
subjects affected / exposed	7 / 117 (5.98%)		
occurrences (all)	7		
Pain			
subjects affected / exposed	10 / 117 (8.55%)		
occurrences (all)	10		
Chest pain			
subjects affected / exposed	8 / 117 (6.84%)		
occurrences (all)	8		
Oedema peripheral			
subjects affected / exposed	16 / 117 (13.68%)		
occurrences (all)	18		
Pyrexia			
subjects affected / exposed	24 / 117 (20.51%)		
occurrences (all)	28		
Asthenia			

subjects affected / exposed	24 / 117 (20.51%)		
occurrences (all)	39		
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	45 / 117 (38.46%)		
occurrences (all)	59		
Cough			
subjects affected / exposed	40 / 117 (34.19%)		
occurrences (all)	51		
Haemoptysis			
subjects affected / exposed	8 / 117 (6.84%)		
occurrences (all)	13		
Oropharyngeal pain			
subjects affected / exposed	6 / 117 (5.13%)		
occurrences (all)	6		
Nasal congestion			
subjects affected / exposed	7 / 117 (5.98%)		
occurrences (all)	10		
Pneumonitis			
subjects affected / exposed	7 / 117 (5.98%)		
occurrences (all)	9		
Psychiatric disorders			
Insomnia			
subjects affected / exposed	7 / 117 (5.98%)		
occurrences (all)	9		
Investigations			
Weight decreased			
subjects affected / exposed	19 / 117 (16.24%)		
occurrences (all)	20		
Blood creatinine increased			
subjects affected / exposed	10 / 117 (8.55%)		
occurrences (all)	13		
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	7 / 117 (5.98%)		
occurrences (all)	11		

Nervous system disorders			
Dizziness			
subjects affected / exposed	14 / 117 (11.97%)		
occurrences (all)	16		
Headache			
subjects affected / exposed	11 / 117 (9.40%)		
occurrences (all)	14		
Neuropathy peripheral			
subjects affected / exposed	7 / 117 (5.98%)		
occurrences (all)	7		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	22 / 117 (18.80%)		
occurrences (all)	28		
Gastrointestinal disorders			
Dry mouth			
subjects affected / exposed	8 / 117 (6.84%)		
occurrences (all)	8		
Abdominal pain			
subjects affected / exposed	14 / 117 (11.97%)		
occurrences (all)	16		
Constipation			
subjects affected / exposed	31 / 117 (26.50%)		
occurrences (all)	36		
Vomiting			
subjects affected / exposed	24 / 117 (20.51%)		
occurrences (all)	27		
Nausea			
subjects affected / exposed	37 / 117 (31.62%)		
occurrences (all)	47		
Diarrhoea			
subjects affected / exposed	24 / 117 (20.51%)		
occurrences (all)	55		
Abdominal pain upper			
subjects affected / exposed	7 / 117 (5.98%)		
occurrences (all)	8		
Skin and subcutaneous tissue disorders			

Pruritus			
subjects affected / exposed	14 / 117 (11.97%)		
occurrences (all)	20		
Rash			
subjects affected / exposed	17 / 117 (14.53%)		
occurrences (all)	20		
Musculoskeletal and connective tissue disorders			
Myalgia			
subjects affected / exposed	13 / 117 (11.11%)		
occurrences (all)	15		
Musculoskeletal chest pain			
subjects affected / exposed	9 / 117 (7.69%)		
occurrences (all)	10		
Arthralgia			
subjects affected / exposed	24 / 117 (20.51%)		
occurrences (all)	28		
Pain in extremity			
subjects affected / exposed	9 / 117 (7.69%)		
occurrences (all)	10		
Back pain			
subjects affected / exposed	14 / 117 (11.97%)		
occurrences (all)	16		
Muscular weakness			
subjects affected / exposed	8 / 117 (6.84%)		
occurrences (all)	9		
Infections and infestations			
Bronchitis			
subjects affected / exposed	11 / 117 (9.40%)		
occurrences (all)	15		
Pneumonia			
subjects affected / exposed	7 / 117 (5.98%)		
occurrences (all)	7		
Sinusitis			
subjects affected / exposed	7 / 117 (5.98%)		
occurrences (all)	10		
Metabolism and nutrition disorders			

Hypophosphataemia subjects affected / exposed occurrences (all)	6 / 117 (5.13%) 9		
Hypercalcaemia subjects affected / exposed occurrences (all)	9 / 117 (7.69%) 12		
Decreased appetite subjects affected / exposed occurrences (all)	46 / 117 (39.32%) 54		
Hypomagnesaemia subjects affected / exposed occurrences (all)	10 / 117 (8.55%) 24		
Dehydration subjects affected / exposed occurrences (all)	10 / 117 (8.55%) 12		
Hyponatraemia subjects affected / exposed occurrences (all)	10 / 117 (8.55%) 16		
Hyperglycaemia subjects affected / exposed occurrences (all)	10 / 117 (8.55%) 16		
Hypoalbuminaemia subjects affected / exposed occurrences (all)	6 / 117 (5.13%) 6		
Hypokalaemia subjects affected / exposed occurrences (all)	7 / 117 (5.98%) 24		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
05 March 2013	Inclusion of non-clinical safety findings related to reproductive toxicology data.
28 March 2013	In the document, BMS-936558 has been replaced by the approved generic name "nivolumab" or the generic name nivolumab has been used in addition to BMS-936558. The clinical trial protocol CA209063 is additionally identified as "CheckMate 063 : CHECKpoint pathway and nivoluMAb clinical Trial Evaluation 063". Modified the primary objective of the study to objective response rate (ORR) as assessed by an independent radiology review committee (IRC) and secondary objective response rate as investigator assessed. This modification is in response to a request of the US FDA. Updated with additional safety information occured in the nivolumab program, related opportunistic infections Related to Immunosuppression. Other changes include clarification of the target population, allowable therapies, and additional clarifications and typographical revisions throughout the protocol.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported