Clinical trial results:
A Single-Arm, Open-Label Phase 2 Study of Nivolumab (BMS-936558) in Subjects with Relapsed or Refractory Follicular Lymphoma (FL) (CheckMate 140: CHECKpoint pathway and nivoluMAb clinical Trial Evaluation 140)

Summary

EudraCT number	2013-003645-42
Trial protocol	GB BE SE ES IT DE FR
Global end of trial date	28 December 2020

Results information

Result version number	v1 (current)
This version publication date	29 December 2021
First version publication date	29 December 2021

Trial information

Trial identification

Sponsor protocol code	CA209-140

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	Chaussée 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	05 March 2021
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	28 December 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the clinical benefit of nivolumab, as measured by independent radiologic review committee (IRRC) assessed objective response rate (ORR) in subjects with FL who have failed therapy with both rituximab and an alkylating agent.

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	26 March 2014
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	Australia: 2
Country: Number of subjects enrolled	Belgium: 7
Country: Number of subjects enrolled	Canada: 4
Country: Number of subjects enrolled	France: 7
Country: Number of subjects enrolled	Italy: 19
Country: Number of subjects enrolled	Norway: 3
Country: Number of subjects enrolled	Singapore: 3
Country: Number of subjects enrolled	Spain: 9
Country: Number of subjects enrolled	United Kingdom: 7
Country: Number of subjects enrolled	United States: 31
Worldwide total number of subjects	92
EEA total number of subjects	45

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)	40
From 65 to 84 years	50
85 years and over	2

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

116 participants were enrolled; 92 received study treatment. Participants were enrolled but not treated because they no longer met study criteria (n=20), withdrew consent (n=1), or for other reasons (n=3).

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	Arm 1: Nivolumab

Arm description:

Nivolumab 3mg/kg intravenously every 2 weeks until disease progression or discontinuation due to toxicity

Arm type	Experimental
Investigational medicinal product name	Nivolumab
Investigational medicinal product code	
Other name	BMS-936558
Pharmaceutical forms	Solvent for solution for infusion, Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Administered intravenously over 60 minutes at 3 mg/kg every 2 weeks

Number of subjects in period 1	Arm 1: Nivolumab
Started	92
Completed	80
Not completed	12
Adverse event, serious fatal	5
Consent withdrawn by subject	3
Other reasons	2
Lost to follow-up	2

Baseline characteristics

Reporting groups	
Reporting group title	Arm 1: Nivolumab
Reporting group description:	
Nivolumab 3mg/kg intravenously every 2 weeks until disease progression or discontinuation due to toxicity	

Reporting group values	Arm 1: Nivolumab	Total	
Number of subjects	92	92	
Age categorical Units: Subjects			
Adults (18-64 years)	40	40	
From 65-84 years	50	50	
85 years and over	2	2	
Age Continuous Units: years			
arithmetic mean	65.2		
standard deviation	± 10.50	-	
Sex: Female, Male Units: Participants			
Female	44	44	
Male	48	48	
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	3	3	
Native Hawaiian or Other Pacific Islander	0	0	
Black or African American	1	1	
White	87	87	
More than one race	0	0	
Unknown or Not Reported	1	1	
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	5	5	
Not Hispanic or Latino	49	49	
Unknown or Not Reported	38	38	

End points

End points reporting groups

Reporting group title	Arm 1: Nivolumab

Reporting group description:

Nivolumab 3mg/kg intravenously every 2 weeks until disease progression or discontinuation due to toxicity

Primary: Overall response rate (ORR) as determined by IRRC

End point title	Overall response rate (ORR) as determined by IRRC[1]

End point description:

ORR is determined by an independent radiologic review committee (IRRC) according to the revised International Working Group Criteria for non-Hodgkin Lymphoma. ORR is defined as the number of subjects with a best overall response (BOR) of complete response (CR) or partial response (PR) and expressed as a percentage of all treated participants. CR=Disappearance of all clinical/radiographic evidence of disease, regression of lymph nodes to normal size, absence of spleen, liver, and bone marrow involvement. PR=Regression of measurable disease and no new sites; no increase in size of liver or spleen. >=50% decrease in SPD of up to 6 largest dominant masses (index lesions); no increase in size of other nodes (non-index lesions)

End point type	Primary

End point timeframe:

From Week 9 until documented disease progression or study discontinuation (assessed up to June 2017, approximately 38 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: Only summary statistics were planned for this endpoint

End point values	Arm 1: Nivolumab			
Subject group type	Reporting group			
Number of subjects analysed	92			
Units: Percentage of participants				
number (confidence interval 95%)	4.3 (1.2 to 10.8)			

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of response (DOR) based on IRRC assessments

End point title	Duration of response (DOR) based on IRRC assessments

End point description:

DOR is defined as the time from first remission (CR or PR) to the date of initial objectively documented progression as determined using the revised International Working Group Criteria for non-Hodgkin Lymphoma, or death due to any cause, whichever occurs first. CR definition includes the complete disappearance of all evidence of disease, the definition of PR includes at least a 50% decrease in sum of the product of the diameters (SPD) of up to six of the largest dominant nodes or nodal masses, and PD is defined as any new lesion or increase by >50% of previously involved sites from nadir, as described in the IWG response criteria

End point type	Secondary

End point timeframe:

From Week 9 until documented disease progression or study discontinuation (assessed up to June 2017, approximately 38 months)

End point values	Arm 1: Nivolumab			
Subject group type	Reporting group			
Number of subjects analysed	92			
Units: months				
median (confidence interval 95%)	10.94 (8.31 to 13.57)			

Statistical analyses

No statistical analyses for this end point

Secondary: Complete remission rate (CRR) based on IRRC assessment

End point title	Complete remission rate (CRR) based on IRRC assessment

End point description:

CRR is defined as the number of subjects with a BOR of CR according to the revised International Working Group Criteria for non-Hodgkin Lymphoma, divided by the number of treated participants and expressed as a percentage. CR=Disappearance of all clinical/radiographic evidence of disease, regression of lymph nodes to normal size, absence of spleen, liver, and bone marrow involvement.

End point type	Secondary

End point timeframe:

From Week 9 until documented disease progression or study discontinuation (assessed up to June 2017, approximately 38 months)

End point values	Arm 1: Nivolumab			
Subject group type	Reporting group			
Number of subjects analysed	92			
Units: Percentage of participants				
number (confidence interval 95%)	1.1 (0.0 to 5.9)			

Statistical analyses

No statistical analyses for this end point

Secondary: Partial remission (PR) rate based on IRRC assessment

End point title	Partial remission (PR) rate based on IRRC assessment

End point description:

PR rate is defined as the number of participants with a best overall response (BOR) of PR according to the 2007 International Working Group (IWG) criteria, based on IRRC assessment, divided by the

number of treated participants and expressed as a percentage. PR=Regression of measurable disease and no new sites; no increase in size of liver or spleen. >=50% decrease in SPD of up to 6 largest dominant masses (index lesions); no increase in size of other nodes (non-index lesions)

End point type	Secondary

End point timeframe:

From Week 9 until documented disease progression or study discontinuation (assessed up to June 2017, approximately 38 months)

End point values	Arm 1: Nivolumab			
Subject group type	Reporting group			
Number of subjects analysed	92			
Units: Percentage of participants				
number (confidence interval 95%)	3.3 (0.7 to 9.2)			

Statistical analyses

No statistical analyses for this end point

Secondary: Progression free survival (PFS) based on IRRC assessment

End point title	Progression free survival (PFS) based on IRRC assessment

End point description:

PFS was summarized descriptively using the Kaplan-Meier (KM) product-limit method. Median values of PFS, along with the two-sided 95% CIs were calculated using a method based on log-log transformation.

End point type	Secondary

End point timeframe:

From Week 9 until documented disease progression or study discontinuation (assessed up to June 2017, approximately 38 months)

End point values	Arm 1: Nivolumab			
Subject group type	Reporting group			
Number of subjects analysed	92			
Units: months				
median (confidence interval 95%)	2.20 (1.91 to 3.58)			

Statistical analyses

No statistical analyses for this end point

Secondary: Overall response rate (ORR) based on investigator assessments

End point title	Overall response rate (ORR) based on investigator assessments

End point description:

ORR is determined by investigator assessments according to the revised International Working Group Criteria for non-Hodgkin Lymphoma. ORR is defined as the number of subjects with a best overall response (BOR) of complete response (CR) or partial response (PR) and is expressed as a percentage of all treated participants. CR=Disappearance of all clinical/radiographic evidence of disease, regression of lymph nodes to normal size, absence of spleen, liver, and bone marrow involvement. PR=Regression of measurable disease and no new sites; no increase in size of liver or spleen. >=50% decrease in SPD of up to 6 largest dominant masses (index lesions); no increase in size of other nodes (non-index lesions)

End point type	Secondary

End point timeframe:

From Week 9 until documented disease progression or study discontinuation (assessed up to June 2017, approximately 38 months)

End point values	Arm 1: Nivolumab			
Subject group type	Reporting group			
Number of subjects analysed	92			
Units: Percentage of participants				
number (confidence interval 95%)	10.9 (5.3 to 19.1)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From first dose to 100 days after last dose of study therapy (up to approximately 6 years 9 months)

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.0

Reporting groups

Reporting group title	Nivolumab (BMS-936558)

Reporting group description:

Subjects with Relapsed or Refractory Follicular Lymphoma were administered 3 milligram/Kilogram Nivolumab over 60 minutes Intravenously every 2 weeks until progression or unacceptable toxicity.

Serious adverse events	Nivolumab (BMS-936558)		
Total subjects affected by serious adverse events			
subjects affected / exposed	46 / 92 (50.00%)		
number of deaths (all causes)	14		
number of deaths resulting from adverse events	3		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Lymphoma			
subjects affected / exposed	1 / 92 (1.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Malignant neoplasm progression			
subjects affected / exposed	8 / 92 (8.70%)		
occurrences causally related to treatment / all	0 / 9		
deaths causally related to treatment / all	0 / 0		
Myelodysplastic syndrome			
subjects affected / exposed	1 / 92 (1.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Squamous cell carcinoma			
subjects affected / exposed	1 / 92 (1.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 92 (1.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General physical health deterioration			
subjects affected / exposed	1 / 92 (1.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Fatigue			
subjects affected / exposed	1 / 92 (1.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Multiple organ dysfunction syndrome			
subjects affected / exposed	1 / 92 (1.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pyrexia			
subjects affected / exposed	6 / 92 (6.52%)		
occurrences causally related to treatment / all	1 / 7		
deaths causally related to treatment / all	0 / 0		
Immune system disorders			
Anaphylactic shock			
subjects affected / exposed	1 / 92 (1.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hypersensitivity			
subjects affected / exposed	1 / 92 (1.09%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Aspiration			

subjects affected / exposed	1 / 92 (1.09%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Acute respiratory failure				
subjects affected / exposed	1 / 92 (1.09%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	1 / 1			
Dyspnoea				
subjects affected / exposed	1 / 92 (1.09%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Immune-mediated pneumonitis				
subjects affected / exposed	1 / 92 (1.09%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Pleural effusion				
subjects affected / exposed	2 / 92 (2.17%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 0			
Pneumonitis				
subjects affected / exposed	1 / 92 (1.09%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory failure				
subjects affected / exposed	1 / 92 (1.09%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Psychiatric disorders				
Confusional state				
subjects affected / exposed	1 / 92 (1.09%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Investigations				

Influenza B virus test positive			
subjects affected / exposed	1 / 92 (1.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Transaminases increased			
subjects affected / exposed	1 / 92 (1.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Infusion related reaction			
subjects affected / exposed	1 / 92 (1.09%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Cardiac failure			
subjects affected / exposed	1 / 92 (1.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac failure congestive			
subjects affected / exposed	1 / 92 (1.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac failure acute			
subjects affected / exposed	1 / 92 (1.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Myocardial infarction			
subjects affected / exposed	1 / 92 (1.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Sciatica			

subjects affected / exposed	1 / 92 (1.09%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Syncope				
subjects affected / exposed	1 / 92 (1.09%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Blood and lymphatic system disorders				
Autoimmune haemolytic anaemia				
subjects affected / exposed	1 / 92 (1.09%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Cytopenia				
subjects affected / exposed	1 / 92 (1.09%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Febrile neutropenia				
subjects affected / exposed	4 / 92 (4.35%)			
occurrences causally related to treatment / all	0 / 5			
deaths causally related to treatment / all	0 / 0			
Pancytopenia				
subjects affected / exposed	1 / 92 (1.09%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
Abdominal discomfort				
subjects affected / exposed	1 / 92 (1.09%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Abdominal pain				
subjects affected / exposed	3 / 92 (3.26%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 0			
Ascites				

subjects affected / exposed	1 / 92 (1.09%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Colitis				
subjects affected / exposed	1 / 92 (1.09%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Constipation				
subjects affected / exposed	1 / 92 (1.09%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Diarrhoea				
subjects affected / exposed	3 / 92 (3.26%)			
occurrences causally related to treatment / all	2 / 3			
deaths causally related to treatment / all	0 / 0			
Diverticulum intestinal haemorrhagic				
subjects affected / exposed	1 / 92 (1.09%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Dysphagia				
subjects affected / exposed	1 / 92 (1.09%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal pain				
subjects affected / exposed	1 / 92 (1.09%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pancreatitis acute				
subjects affected / exposed	1 / 92 (1.09%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Intestinal obstruction				

subjects affected / exposed	1 / 92 (1.09%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Small intestinal obstruction				
subjects affected / exposed	1 / 92 (1.09%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Vomiting				
subjects affected / exposed	1 / 92 (1.09%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Skin and subcutaneous tissue disorders				
Erythema multiforme				
subjects affected / exposed	1 / 92 (1.09%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	1 / 1			
Rash				
subjects affected / exposed	1 / 92 (1.09%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Toxic epidermal necrolysis				
subjects affected / exposed	1 / 92 (1.09%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	1 / 1			
Renal and urinary disorders				
Acute kidney injury				
subjects affected / exposed	1 / 92 (1.09%)			
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 / 92 (1.09%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

Muscular weakness				
subjects affected / exposed	1 / 92 (1.09%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Appendicitis				
subjects affected / exposed	1 / 92 (1.09%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Bacteraemia				
subjects affected / exposed	2 / 92 (2.17%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Erysipelas				
subjects affected / exposed	1 / 92 (1.09%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Fungal infection				
subjects affected / exposed	1 / 92 (1.09%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Herpes zoster				
subjects affected / exposed	2 / 92 (2.17%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Lower respiratory tract infection				
subjects affected / exposed	3 / 92 (3.26%)			
occurrences causally related to treatment / all	1 / 3			
deaths causally related to treatment / all	0 / 0			
Pneumonia				
subjects affected / exposed	2 / 92 (2.17%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Pulmonary sepsis				

subjects affected / exposed	1 / 92 (1.09%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pyelonephritis				
subjects affected / exposed	1 / 92 (1.09%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Skin infection				
subjects affected / exposed	2 / 92 (2.17%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Staphylococcal sepsis				
subjects affected / exposed	1 / 92 (1.09%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Urinary tract infection				
subjects affected / exposed	1 / 92 (1.09%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Viral infection				
subjects affected / exposed	1 / 92 (1.09%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Metabolism and nutrition disorders				
Dehydration				
subjects affected / exposed	1 / 92 (1.09%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hypercalcaemia				
subjects affected / exposed	1 / 92 (1.09%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hyperglycaemia				

subjects affected / exposed	2 / 92 (2.17%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Hypokalaemia			
subjects affected / exposed	1 / 92 (1.09%)		
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 (BMS-936558)		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	89 / 92 (96.74%)		
Nervous system disorders			
Dizziness			
subjects affected / exposed	7 / 92 (7.61%)		
occurrences (all)	9		
Headache			
subjects affected / exposed	5 / 92 (5.43%)		
occurrences (all)	5		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	15 / 92 (16.30%)		
occurrences (all)	27		
Neutropenia			
subjects affected / exposed	10 / 92 (10.87%)		
occurrences (all)	24		
Thrombocytopenia			
subjects affected / exposed	8 / 92 (8.70%)		
occurrences (all)	16		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	9 / 92 (9.78%)		
occurrences (all)	10		
Fatigue			

subjects affected / exposed	23 / 92 (25.00%)		
occurrences (all)	44		
Oedema peripheral			
subjects affected / exposed	10 / 92 (10.87%)		
occurrences (all)	12		
Pyrexia			
subjects affected / exposed	25 / 92 (27.17%)		
occurrences (all)	31		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	15 / 92 (16.30%)		
occurrences (all)	24		
Constipation			
subjects affected / exposed	14 / 92 (15.22%)		
occurrences (all)	19		
Diarrhoea			
subjects affected / exposed	22 / 92 (23.91%)		
occurrences (all)	41		
Dysphagia			
subjects affected / exposed	5 / 92 (5.43%)		
occurrences (all)	6		
Nausea			
subjects affected / exposed	23 / 92 (25.00%)		
occurrences (all)	35		
Vomiting			
subjects affected / exposed	12 / 92 (13.04%)		
occurrences (all)	19		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	25 / 92 (27.17%)		
occurrences (all)	40		
Dyspnoea			
subjects affected / exposed	13 / 92 (14.13%)		
occurrences (all)	17		
Oropharyngeal pain			

subjects affected / exposed occurrences (all)	5 / 92 (5.43%) 8		
Skin and subcutaneous tissue disorders Pruritus subjects affected / exposed occurrences (all) Rash subjects affected / exposed occurrences (all) Skin lesion subjects affected / exposed occurrences (all)	 11 / 92 (11.96%) 15 8 / 92 (8.70%) 12 5 / 92 (5.43%) 6		
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) Back pain subjects affected / exposed occurrences (all) Myalgia subjects affected / exposed occurrences (all) Muscle spasms subjects affected / exposed occurrences (all)	 6 / 92 (6.52%) 10 11 / 92 (11.96%) 12 6 / 92 (6.52%) 8 5 / 92 (5.43%) 7		
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all) Pneumonia subjects affected / exposed occurrences (all) Upper respiratory tract infection subjects affected / exposed occurrences (all) Urinary tract infection	 8 / 92 (8.70%) 11 6 / 92 (6.52%) 7 11 / 92 (11.96%) 14		

subjects affected / exposed occurrences (all)	9 / 92 (9.78%) 15		
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all) Hypokalaemia subjects affected / exposed occurrences (all)	 14 / 92 (15.22%) 17 6 / 92 (6.52%) 18		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
06 December 2013	The exclusion criterion has been added to exclude the subjects who received chest radiation </= 24 weeks prior to first dose of the study drug.
23 July 2014	Removes the interim analyses and extends the duration of follow-up required for all subjects prior to performing the final analysis of the primary endpoint.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported