Clinical trial results:
A Randomized Open-Label Phase 3 Trial of BMS-936558 (Nivolumab) Versus Investigator's Choice in Advanced (Unresectable or Metastatic) Melanoma Patients Progressing Post Anti-CTLA-4 Therapy

Summary

EudraCT number	2012-001828-35
Trial protocol	BE NL AT GB DE ES IT DK
Global end of trial date	29 December 2020

Results information

Result version number	v1 (current)
This version publication date	03 December 2021
First version publication date	03 December 2021

Trial information

Trial identification

Sponsor protocol code	CA209-037

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	29 December 2020
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	29 December 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Assess efficacy of objective response rate (ORR) and overall survival (OS) of Nivolumab versus Investigator's Choice in Advanced Melanoma patients progressing post anti-CTLA-4 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	21 December 2012
Long term follow-up planned	Yes
Long term follow-up rationale	Efficacy
Long term follow-up duration	5 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Austria: 10
Country: Number of subjects enrolled	Belgium: 23
Country: Number of subjects enrolled	Brazil: 5
Country: Number of subjects enrolled	Canada: 23
Country: Number of subjects enrolled	Denmark: 11
Country: Number of subjects enrolled	France: 31
Country: Number of subjects enrolled	Germany: 48
Country: Number of subjects enrolled	Israel: 2
Country: Number of subjects enrolled	Italy: 32
Country: Number of subjects enrolled	Netherlands: 5
Country: Number of subjects enrolled	Spain: 5
Country: Number of subjects enrolled	Switzerland: 3
Country: Number of subjects enrolled	United Kingdom: 43
Country: Number of subjects enrolled	United States: 164
Worldwide total number of subjects	405
EEA total number of subjects	165

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)	257
From 65 to 84 years	143
85 years and over	5

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

405 participants randomized and 370 treated.

Period 1

Period 1 title	Pre-Treatment
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 IV Q2W

Arm type	Experimental
Investigational medicinal product name	BMS-936558 (Nivolumab)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

3 mg/kg IV over 60 minutes Q2W

Arm title	Investigator\'s Choice (Dacarbazine or Carboplatin+Paclitaxel)

Arm description:

Dacarbazine: 1000 mg/m^2 IV over 30 to 60 minutes Q3W, or Carboplatin: Area under the concentration-time curve (AUC) 6 IV over 30 minutes Q3W, and Paclitaxel: 175 mg/m^2 IV over 180 minutes Q3W

Arm type	Active comparator
Investigational medicinal product name	Dacarbazine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for intravesical solution/solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

1000 mg/m^2 IV Q3W

Investigational medicinal product name	Paclitaxel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

175 mg/m^2 IV over 180 minutes Q3W

Investigational medicinal product name	Carboplatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection

Routes of administration	Intravenous use

Dosage and administration details:

Area under the concentration-time curve (AUC) 6 IV over 30 minutes Q3W

Number of subjects in period 1	Nivolumab	Investigator\'s Choice (Dacarbazine or Carboplatin+Paclitaxel)
Started	272	133
Completed	268	102
Not completed	4	31
Consent withdrawn by subject	1	16
Subject no longer met study criteria	2	2
Subject request to discontinue Study treatment	-	13
Poor/Non-compliance	1	-

Period 2

Period 2 title	Treatment
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 IV Q2W

Arm type	Experimental
Investigational medicinal product name	BMS-936558 (Nivolumab)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

3 mg/kg IV over 60 minutes Q2W

Arm title	Investigator\'s Choice (Dacarbazine or Carboplatin+Paclitaxel)

Arm description:

Dacarbazine: 1000 mg/m^2 IV over 30 to 60 minutes Q3W, or Carboplatin: Area under the concentration-time curve (AUC) 6 IV over 30 minutes Q3W, and Paclitaxel: 175 mg/m^2 IV over 180 minutes Q3W

Arm type	Active comparator
Investigational medicinal product name	Dacarbazine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for intravesical solution/solution for injection
Routes of administration	Intravenous use
Dosage and administration details: 1000 mg/m^2 IV Q3W	
Investigational medicinal product name	Paclitaxel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use
Dosage and administration details: 175 mg/m^2 IV over 180 minutes Q3W	
Investigational medicinal product name	Carboplatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use
Dosage and administration details: Area under the concentration-time curve (AUC) 6 IV over 30 minutes Q3W	

Number of subjects in period 2	Nivolumab	Investigator\'s Choice (Dacarbazine or Carboplatin+Paclitaxel)
Started	268	102
Completed	0	0
Not completed	268	102
Subject withdrew consent	4	2
Maximum Clinical Benefit	9	3
Subject no longer met study criteria	4	-
Adverse Event unrelated to Study Drug	6	3
Subject request to discontinue Study treatment	26	7
Poor/Non-compliance	2	-
Other reasons	6	2
Study Drug Toxicity	19	11
Disease Progression	192	74

Baseline characteristics

Reporting groups	
Reporting group title	Nivolumab
Reporting group description:	
Nivolumab 3 mg/kg IV Q2W	
Reporting group title	Investigator\'s Choice (Dacarbazine or Carboplatin+Paclitaxel)
Reporting group description:	
Dacarbazine: 1000 mg/m^2 IV over 30 to 60 minutes Q3W, or Carboplatin: Area under the concentration-time curve (AUC) 6 IV over 30 minutes Q3W, and Paclitaxel: 175 mg/m^2 IV over 180 minutes Q3W	

Reporting group values	Nivolumab	Investigator\'s Choice (Dacarbazine or Carboplatin+Paclitaxel)	Total
Number of subjects	272	133	405
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	177	80	257
From 65-84 years	91	52	143
85 years and over	4	1	5
Age Continuous			
Units: years			
arithmetic mean	58.7	60.3	
standard deviation	± 14.1	± 12.4	-
Sex: Female, Male			
Units:			
Female	96	48	144
Male	176	85	261
Race/Ethnicity, Customized			
Units: Subjects			
White	269	129	398
Black or African American	1	2	3
Asian	2	0	2
American Indian or Alaska Native	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Other	0	2	2
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	4	1	5
Not Hispanic or Latino	116	61	177

Unknown or Not Reported	152	71	223

End points

End points reporting groups

Reporting group title	Nivolumab
Reporting group description: Nivolumab 3 mg/kg IV Q2W	
Reporting group title	Investigator\'s Choice (Dacarbazine or Carboplatin+Paclitaxel)
Reporting group description: Dacarbazine: 1000 mg/m^2 IV over 30 to 60 minutes Q3W, or Carboplatin: Area under the concentration-time curve (AUC) 6 IV over 30 minutes Q3W, and Paclitaxel: 175 mg/m^2 IV over 180 minutes Q3W	
Reporting group title	Nivolumab
Reporting group description: Nivolumab 3 mg/kg IV Q2W	
Reporting group title	Investigator\'s Choice (Dacarbazine or Carboplatin+Paclitaxel)
Reporting group description: Dacarbazine: 1000 mg/m^2 IV over 30 to 60 minutes Q3W, or Carboplatin: Area under the concentration-time curve (AUC) 6 IV over 30 minutes Q3W, and Paclitaxel: 175 mg/m^2 IV over 180 minutes Q3W	

Primary: Objective Response Rate (ORR)

End point title	Objective Response Rate (ORR)[1]
End point description: Objective response rate (ORR) per Independent Review Committee (IRC) is defined as the number of participants with a best overall response (BOR) of complete response (CR) or partial response (PR) divided by the number of randomized participants using RECIST 1.1	
End point type	Primary
End point timeframe: From date of randomization to the date of objectively documented progression, date of death, or the date of subsequent therapy (Up to 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 planned for this endpoint

End point values	Nivolumab	Investigator\'s Choice (Dacarbazine or Carboplatin+Paclitaxel)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	272	133		
Units: Percentage of participants				
number (confidence interval 95%)	27.2 (22.0 to 32.9)	9.8 (5.3 to 16.1)		

Statistical analyses

No statistical analyses for this end point

Primary: Overall Survival (OS)

End point title	Overall Survival (OS)

End point description:

Overall Survival (OS) was defined the time between the date of randomization to the date of death. For participants without documentation of death, OS was censored on the last date the participant was known to be alive. Unit of measure (months) is the median survival time.

End point type	Primary

End point timeframe:

Up to 96 months

End point values	Nivolumab	Investigator\'s Choice (Dacarbazine or Carboplatin+Paclitaxel)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	272	133		
Units: Months				
number (confidence interval 95%)	15.74 (12.88 to 19.88)	14.39 (11.66 to 18.17)		

Statistical analyses

Statistical analysis title	Hazard Ratio (HR)

Statistical analysis description:

Hazard Ratio is Nivolumab 3 mg/kg (IV) over Investigator's Choice (Dacarbazine or Carboplatin+Paclitaxel)

Comparison groups	Nivolumab v Investigator\'s Choice (Dacarbazine or Carboplatin+Paclitaxel)
Number of subjects included in analysis	405
Analysis specification	Pre-specified
Analysis type	superiority[2]
Parameter estimate	Hazard ratio (HR)
Point estimate	0.86
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.68
upper limit	1.08

Notes:

[2] - From stratified cox proportional hazard model with treatment group as a single covariate, stratified by BRAF status, prior anti-CTLA-4 benefit, and PD-L1 status (IVRS source)

Secondary: Progression Free Survival (PFS)

End point title	Progression Free Survival (PFS)

End point description:

Progression Free Survival (PFS) is defined as the time from randomization to the date of the first documented progression, as determined by the Independent Review Committee (IRC) using RECIST 1.1, or death due to any cause, whichever occurs first. Participants who died without a reported progression were considered to have progressed on the date of their death. Participants who did not progress or die were censored on the date of their last evaluable tumor assessment prior to or on the date of initiation of the subsequent anti-cancer therapy. Unit of measure (months) is the median survival time.

End point type	Secondary

End point timeframe:

From the date of randomization to the date of the first documented progression or death (Up to approximately 38 months)

End point values	Nivolumab	Investigator\'s Choice (Dacarbazine or Carboplatin+Paclitaxel)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	272	133		
Units: months				
number (confidence interval 95%)	3.12 (2.33 to 3.52)	3.65 (2.30 to 5.29)		

Statistical analyses

Statistical analysis title	Hazard Ratio (HR)

Statistical analysis description:

Hazard Ratio is Nivolumab 3 mg/kg (IV) over Investigator's Choice (Dacarbazine or Carboplatin+Paclitaxel)

Comparison groups	Nivolumab v Investigator\'s Choice (Dacarbazine or Carboplatin+Paclitaxel)
Number of subjects included in analysis	405
Analysis specification	Pre-specified
Analysis type	superiority[3]
Parameter estimate	Hazard ratio (HR)
Point estimate	1.03
Confidence interval	
level	95.1 %
sides	2-sided
lower limit	0.78
upper limit	1.36

Notes:

[3] - From stratified cox proportional hazard model with treatment group as a single covariate, stratified by BRAF status, prior anti-CTLA-4 benefit, and PD-L1 status (IVRS source)

Secondary: Objective Response Rate (ORR) by Baseline PD-L1 Expression

End point title	Objective Response Rate (ORR) by Baseline PD-L1 Expression

End point description:

Objective Response Rate (ORR) is defined as the number of participants with a Best Overall Response (BOR) of complete response (CR) or partial response (PR) divided by number of randomized

participants. PD-L1 expression evaluated for ORR.

End point type	Secondary

End point timeframe:

From date of randomization to the date of objectively documented progression or the date of subsequent therapy (Up to approximately 38 months)

End point values	Nivolumab	Investigator\'s Choice (Dacarbazine or Carboplatin+Paclitaxel)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	267[4]	131[5]		
Units: Percentage of participants				
number (confidence interval 95%)				
<5% PD-L1 expression	15.3 (9.7 to 22.5)	13.8 (6.1 to 25.4)		
>=5% PD-L1 expression	43.2 (33.9 to 53.0)	12.2 (4.1 to 26.2)		

Notes:

[4] - <5% PD-L1 expression = 137 subjects
>=5% PD-L1 expression = 111 subjects
[5] - <5% PD-L1 expression = 58 subjects
>=5% PD-L1 expression = 41 subjects

Statistical analyses

Statistical analysis title	Odds Ratio (OR)

Statistical analysis description:

For <5% PD-L1 expression. Ratio of Nivolumab over Investigator's Choice

Comparison groups	Nivolumab v Investigator\'s Choice (Dacarbazine or Carboplatin+Paclitaxel)
Number of subjects included in analysis	398
Analysis specification	Pre-specified
Analysis type	superiority[6]
Parameter estimate	Odds ratio (OR)
Point estimate	1.13
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.44
upper limit	3.16

Notes:

[6] - Subjects in this analysis are 137 from Nivolumab treatment and 58 from IC treatment

Statistical analysis title	Odds Ratio (OR)

Statistical analysis description:

For >=5% PD-L1 expression. Ratio of Nivolumab over Investigator's Choice

Comparison groups	Nivolumab v Investigator\'s Choice (Dacarbazine or Carboplatin+Paclitaxel)

Number of subjects included in analysis	398
Analysis specification	Pre-specified
Analysis type	superiority[7]
Parameter estimate	Odds ratio (OR)
Point estimate	5.49
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.92
upper limit	19.08

Notes:

[7] - Subjects in this analysis are 111 from Nivolumab treatment and 41 from IC treatment

Secondary: Overall Survival (OS) by PD-L1 Expression

End point title	Overall Survival (OS) by PD-L1 Expression

End point description:

Overall Survival (OS) by PD-L1 expression was defined the time between the date of randomization to the date of death. For participants without documentation of death, OS was censored on the last date the participant was known to be alive.

End point type	Secondary

End point timeframe:

Up to 96 months

End point values	Nivolumab	Investigator\'s Choice (Dacarbazine or Carboplatin+Paclitaxel)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	272[8]	133[9]		
Units: Months				
median (confidence interval 95%)				
PD-L1 Positive	31.44 (20.57 to 46.69)	16.72 (11.83 to 31.44)		
PD-L1 Negative/Indeterminate	11.14 (7.72 to 13.21)	11.76 (8.05 to 17.81)		

Notes:

[8] - PD-L1 Positive = 135
PD-L1 Negative/Indeterminate = 137
[9] - PD-L1 Positive = 67
PD-L1 Negative/Indeterminate = 66

Statistical analyses

Statistical analysis title	Hazard Ratio (HR)

Statistical analysis description:

PD-L1 Positive

Comparison groups	Nivolumab v Investigator\'s Choice (Dacarbazine or Carboplatin+Paclitaxel)

Number of subjects included in analysis	405
Analysis specification	Pre-specified
Analysis type	superiority[10]
Parameter estimate	Hazard ratio (HR)
Point estimate	0.71
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.5
upper limit	1.01

Notes:

[10] - Subjects in this analysis are 135 from Nivolumab treatment and 67 from IC treatment

Statistical analysis title	Hazard Ratio (HR)

Statistical analysis description:

PD-L1 Negative/Indeterminate

Comparison groups	Nivolumab v Investigator\'s Choice (Dacarbazine or Carboplatin+Paclitaxel)
Number of subjects included in analysis	405
Analysis specification	Pre-specified
Analysis type	superiority[11]
Parameter estimate	Hazard ratio (HR)
Point estimate	1.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.75
upper limit	1.41

Notes:

[11] - Subjects in this analysis are 137 from Nivolumab treatment and 66 from IC treatment

Secondary: Mean change from baseline in Health-related Quality of Life (HRQoL)

End point title	Mean change from baseline in Health-related Quality of Life (HRQoL)

End point description:

Health-related Quality of Life (HRQoL) was assessed with the EORTC QLQ-C30 questionnaire, which is the most commonly used quality-of-life instrument in oncology trials. The instrument’s 30 items were divided among 5 functional scales (physical, role, cognitive, emotional, and social), 9 symptom scales (fatigue, pain, nausea/vomiting, dyspnea, insomnia, appetite loss, constipation, diarrhea, and financial difficulties), and a global health/quality of life scale. Raw scores for the EORTC QLQ-C30 were transformed to a 0-100 metric. Higher scores for all functional scales and Global Health Status=better HRQoL Increase from baseline indicates improvement in HRQoL. Lower scores for symptom scales=better HRQoL Decline from baseline for symptom scales =improvement in symptoms compared to baseline. A 10 point difference on a 100 point scale between treatments was considered clinically significant.

End point type	Secondary

End point timeframe:

From Baseline (Day1) to second Follow-Up (Up to 96 months)

End point values	Nivolumab	Investigator\'s Choice (Dacarbazine or Carboplatin+Paclitaxel)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	272	133		
Units: Units on a scale				
arithmetic mean (standard deviation)				
Physical Functioning Follow-Up 1	-7.97 (± 20.49)	-12.73 (± 21.47)		
Physical Functioning Follow-Up 2	-3.66 (± 16.05)	-7.14 (± 16.02)		
Role Functioning Follow-Up 1	-14.94 (± 31.13)	-15.91 (± 29.76)		
Role Functioning Follow-Up 2	-7.80 (± 25.56)	-8.33 (± 21.52)		
Emotional Functioning Follow-Up 1	-5.09 (± 21.59)	-15.48 (± 24.48)		
Emotional Functioning Follow-Up 2	-0.94 (± 19.15)	-5.36 (± 25.98)		
Cognitive Functioning Follow-Up 1	-7.58 (± 16.79)	-7.94 (± 17.17)		
Cognitive Functioning Follow-Up 2	-3.49 (± 15.43)	-1.19 (± 13.55)		
Social Functioning Follow-Up 1	-8.66 (± 29.45)	-18.25 (± 26.82)		
Social Functioning Follow-Up 2	-1.61 (± 29.52)	-4.17 (± 24.69)		
Global Health Status Follow-Up 1	-8.23 (± 22.44)	-10.71 (± 17.71)		
Global Health Status Follow-Up 2	-1.61 (± 18.53)	-3.27 (± 12.07)		
Dyspnea Follow-Up 1	6.06 (± 27.96)	16.67 (± 24.67)		
Dyspnea Follow-Up 2	5.91 (± 22.20)	7.14 (± 24.61)		
Insomnia Follow-Up 1	3.46 (± 32.26)	0.00 (± 30.86)		
Insomnia Follow-Up 2	-4.84 (± 25.50)	0.00 (± 30.09)		
Apatite loss Follow-Up 1	6.93 (± 28.79)	13.64 (± 24.47)		
Apatite loss Follow-Up 2	5.91 (± 30.49)	2.38 (± 22.09)		
Constipation Follow-Up 1	7.36 (± 28.93)	0.00 (± 23.57)		
Constipation Follow-Up 2	2.15 (± 22.48)	-2.38 (± 29.99)		
Diarrhea Follow-Up 1	-0.43 (± 19.86)	6.35 (± 22.65)		
Diarrhea Follow-Up 2	1.08 (± 20.88)	1.19 (± 16.93)		
Financial Difficulties Follow-Up 1	-1.73 (± 25.87)	4.76 (± 39.84)		
Financial Difficulties Follow-Up 2	-1.08 (± 22.56)	-2.38 (± 28.59)		
Fatigue Follow-Up 1	8.95 (± 23.78)	15.66 (± 28.00)		
Fatigue Follow-Up 2	4.84 (± 22.55)	7.14 (± 21.85)		
Nausea and Vomiting Follow-Up 1	2.81 (± 17.19)	10.61 (± 25.48)		
Nausea and Vomiting Follow-Up 2	0.00 (± 15.39)	2.98 (± 18.73)		
Pain Follow-Up 1	6.06 (± 31.17)	6.82 (± 25.02)		

Pain Follow-Up 2	5.38 (± 24.84)	-1.79 (± 14.59)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

AEs and deaths collected were reported between first dose and 30 days after last dose of study therapy

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.1

Reporting groups

Reporting group title	Investigator Choice (Dacarbazine or Carboplatin+Paclitaxel)

Reporting group description:

Subjects with Advanced Unresectable Melanoma/Advanced Metastatic Melanoma were administered choice of either Dacarbazine at a dose of 1000 milligram/per square meter (mg/m2) IV between 30 to 60 minutes every 3 weeks (Q3W) or carboplatin (AUC 6) at a dose of 175 mg/m2 IV over 30 minutes and paclitaxel at a dose of 175 mg/m2 IV over 180 minutes Q3W until disease progression or treatment discontinuation or until end of the study treatment.

Reporting group title	BMS-936558A (Nivolumab)

Reporting group description:

Subjects with Advanced Unresectable Melanoma/Advanced Metastatic Melanoma were administered BMS-936558A at a dose of 3 milligram/kilogram (mg/kg) intravenously (IV) over 60 minutes every 2 weeks (Q2W) until disease progression or unacceptable toxicity or until end of the study treatment.

Serious adverse events	Investigator Choice (Dacarbazine or Carboplatin+Paclitaxel)	BMS-936558A (Nivolumab)	
Total subjects affected by serious adverse events			
subjects affected / exposed	24 / 102 (23.53%)	162 / 268 (60.45%)	
number of deaths (all causes)	3	30	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cancer pain			
subjects affected / exposed	0 / 102 (0.00%)	3 / 268 (1.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Basal cell carcinoma			
subjects affected / exposed	0 / 102 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Keratoacanthoma			

subjects affected / exposed	0 / 102 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malignant melanoma			
subjects affected / exposed	1 / 102 (0.98%)	3 / 268 (1.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Melanoma recurrent			
subjects affected / exposed	0 / 102 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malignant neoplasm progression			
subjects affected / exposed	5 / 102 (4.90%)	39 / 268 (14.55%)	
occurrences causally related to treatment / all	0 / 7	0 / 49	
deaths causally related to treatment / all	0 / 4	0 / 30	
Metastases to adrenals			
subjects affected / exposed	0 / 102 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastases to pleura			
subjects affected / exposed	0 / 102 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastatic malignant melanoma			
subjects affected / exposed	0 / 102 (0.00%)	5 / 268 (1.87%)	
occurrences causally related to treatment / all	0 / 0	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 1	
Neoplasm malignant			
subjects affected / exposed	0 / 102 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Parathyroid tumour benign			

subjects affected / exposed	0 / 102 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostate cancer			
subjects affected / exposed	0 / 102 (0.00%)	2 / 268 (0.75%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin neoplasm bleeding			
subjects affected / exposed	1 / 102 (0.98%)	0 / 268 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous cell carcinoma			
subjects affected / exposed	0 / 102 (0.00%)	4 / 268 (1.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous cell carcinoma of skin			
subjects affected / exposed	0 / 102 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tonsil cancer			
subjects affected / exposed	0 / 102 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tumour associated fever			
subjects affected / exposed	1 / 102 (0.98%)	0 / 268 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tumour pain			
subjects affected / exposed	0 / 102 (0.00%)	2 / 268 (0.75%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tumour fistulisation			

subjects affected / exposed	0 / 102 (0.00%)	2 / 268 (0.75%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 102 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Embolism			
subjects affected / exposed	0 / 102 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertension			
subjects affected / exposed	0 / 102 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypotension			
subjects affected / exposed	1 / 102 (0.98%)	3 / 268 (1.12%)	
occurrences causally related to treatment / all	1 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 1	
Peripheral embolism			
subjects affected / exposed	1 / 102 (0.98%)	0 / 268 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Superior vena cava syndrome			
subjects affected / exposed	0 / 102 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 102 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Fatigue			
subjects affected / exposed	2 / 102 (1.96%)	2 / 268 (0.75%)	
occurrences causally related to treatment / all	1 / 2	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gait disturbance			
subjects affected / exposed	0 / 102 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Non-cardiac chest pain			
subjects affected / exposed	0 / 102 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infusion site extravasation			
subjects affected / exposed	0 / 102 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General physical health deterioration			
subjects affected / exposed	0 / 102 (0.00%)	4 / 268 (1.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain			
subjects affected / exposed	1 / 102 (0.98%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pelvic mass			
subjects affected / exposed	0 / 102 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	2 / 102 (1.96%)	4 / 268 (1.49%)	
occurrences causally related to treatment / all	2 / 3	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ulcer			

subjects affected / exposed	0 / 102 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 102 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	3 / 102 (2.94%)	5 / 268 (1.87%)	
occurrences causally related to treatment / all	0 / 3	1 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 102 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemoptysis			
subjects affected / exposed	0 / 102 (0.00%)	2 / 268 (0.75%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Interstitial lung disease			
subjects affected / exposed	0 / 102 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoxia			
subjects affected / exposed	0 / 102 (0.00%)	2 / 268 (0.75%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pleural effusion			
subjects affected / exposed	1 / 102 (0.98%)	2 / 268 (0.75%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

Pulmonary embolism			
subjects affected / exposed	0 / 102 (0.00%)	2 / 268 (0.75%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonitis			
subjects affected / exposed	0 / 102 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Burnout syndrome			
subjects affected / exposed	0 / 102 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Confusional state			
subjects affected / exposed	0 / 102 (0.00%)	3 / 268 (1.12%)	
occurrences causally related to treatment / all	0 / 0	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 102 (0.00%)	2 / 268 (0.75%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 102 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 102 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ejection fraction abnormal			
subjects affected / exposed	0 / 102 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Influenza B virus test positive			
subjects affected / exposed	0 / 102 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic enzyme increased			
subjects affected / exposed	0 / 102 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liver function test abnormal			
subjects affected / exposed	0 / 102 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liver function test increased			
subjects affected / exposed	0 / 102 (0.00%)	2 / 268 (0.75%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Femur fracture			
subjects affected / exposed	0 / 102 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Humerus fracture			
subjects affected / exposed	0 / 102 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infusion related reaction			
subjects affected / exposed	0 / 102 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative ileus			
subjects affected / exposed	0 / 102 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Open fracture			
subjects affected / exposed	0 / 102 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Radiation necrosis			
subjects affected / exposed	0 / 102 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rib fracture			
subjects affected / exposed	0 / 102 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal fracture			
subjects affected / exposed	0 / 102 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subdural haematoma			
subjects affected / exposed	0 / 102 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Toxicity to various agents			
subjects affected / exposed	1 / 102 (0.98%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular access site thrombosis			
subjects affected / exposed	0 / 102 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound dehiscence			
subjects affected / exposed	0 / 102 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			

Acute myocardial infarction			
subjects affected / exposed	0 / 102 (0.00%)	1 / 268 (0.37%)	
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	0 / 102 (0.00%)	4 / 268 (1.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 1	
Atrial flutter			
subjects affected / exposed	0 / 102 (0.00%)	2 / 268 (0.75%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac arrest			
subjects affected / exposed	0 / 102 (0.00%)	3 / 268 (1.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cardiac failure			
subjects affected / exposed	0 / 102 (0.00%)	1 / 268 (0.37%)	
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	0 / 102 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Myocardial infarction			
subjects affected / exposed	0 / 102 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericarditis			
subjects affected / exposed	0 / 102 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinus tachycardia			

subjects affected / exposed	0 / 102 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular arrhythmia			
subjects affected / exposed	0 / 102 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Aphasia			
subjects affected / exposed	0 / 102 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Autoimmune neuropathy			
subjects affected / exposed	0 / 102 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brain oedema			
subjects affected / exposed	0 / 102 (0.00%)	1 / 268 (0.37%)	
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	0 / 102 (0.00%)	2 / 268 (0.75%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Demyelination			
subjects affected / exposed	0 / 102 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dizziness			
subjects affected / exposed	0 / 102 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhage intracranial			

subjects affected / exposed	0 / 102 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Headache			
subjects affected / exposed	0 / 102 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seizure			
subjects affected / exposed	0 / 102 (0.00%)	2 / 268 (0.75%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient ischaemic attack			
subjects affected / exposed	1 / 102 (0.98%)	0 / 268 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Status epilepticus			
subjects affected / exposed	0 / 102 (0.00%)	1 / 268 (0.37%)	
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			
Blood loss anaemia			
subjects affected / exposed	0 / 102 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anaemia			
subjects affected / exposed	2 / 102 (1.96%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	1 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile neutropenia			
subjects affected / exposed	2 / 102 (1.96%)	0 / 268 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphadenopathy			

subjects affected / exposed	0 / 102 (0.00%)	2 / 268 (0.75%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Splenic haematoma			
subjects affected / exposed	0 / 102 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			
subjects affected / exposed	1 / 102 (0.98%)	0 / 268 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Splenic lesion			
subjects affected / exposed	0 / 102 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Retinal detachment			
subjects affected / exposed	0 / 102 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 102 (0.00%)	5 / 268 (1.87%)	
occurrences causally related to treatment / all	0 / 0	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain upper			
subjects affected / exposed	0 / 102 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ascites			
subjects affected / exposed	0 / 102 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis			

subjects affected / exposed	0 / 102 (0.00%)	2 / 268 (0.75%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Constipation			
subjects affected / exposed	0 / 102 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticular perforation			
subjects affected / exposed	0 / 102 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	2 / 102 (1.96%)	3 / 268 (1.12%)	
occurrences causally related to treatment / all	2 / 2	2 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysphagia			
subjects affected / exposed	0 / 102 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematemesis			
subjects affected / exposed	0 / 102 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inguinal hernia			
subjects affected / exposed	0 / 102 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			
subjects affected / exposed	1 / 102 (0.98%)	2 / 268 (0.75%)	
occurrences causally related to treatment / all	1 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower gastrointestinal haemorrhage			

subjects affected / exposed	0 / 102 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis			
subjects affected / exposed	0 / 102 (0.00%)	2 / 268 (0.75%)	
occurrences causally related to treatment / all	0 / 0	2 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal obstruction			
subjects affected / exposed	0 / 102 (0.00%)	3 / 268 (1.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper gastrointestinal haemorrhage			
subjects affected / exposed	0 / 102 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	3 / 102 (2.94%)	2 / 268 (0.75%)	
occurrences causally related to treatment / all	3 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Hepatic haemorrhage			
subjects affected / exposed	0 / 102 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis			
subjects affected / exposed	0 / 102 (0.00%)	2 / 268 (0.75%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatocellular injury			
subjects affected / exposed	0 / 102 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			

Skin haemorrhage			
subjects affected / exposed	1 / 102 (0.98%)	0 / 268 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	2 / 102 (1.96%)	0 / 268 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hydronephrosis			
subjects affected / exposed	0 / 102 (0.00%)	2 / 268 (0.75%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephrolithiasis			
subjects affected / exposed	0 / 102 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal failure			
subjects affected / exposed	0 / 102 (0.00%)	2 / 268 (0.75%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal impairment			
subjects affected / exposed	0 / 102 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tubulointerstitial nephritis			
subjects affected / exposed	0 / 102 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Adrenal haemorrhage			
subjects affected / exposed	0 / 102 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Adrenal insufficiency			
subjects affected / exposed	0 / 102 (0.00%)	2 / 268 (0.75%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypothyroidism			
subjects affected / exposed	0 / 102 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 102 (0.98%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthritis			
subjects affected / exposed	0 / 102 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Back pain			
subjects affected / exposed	2 / 102 (1.96%)	6 / 268 (2.24%)	
occurrences causally related to treatment / all	0 / 2	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Flank pain			
subjects affected / exposed	1 / 102 (0.98%)	0 / 268 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lumbar spinal stenosis			
subjects affected / exposed	0 / 102 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoarthritis			
subjects affected / exposed	0 / 102 (0.00%)	4 / 268 (1.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	

Spondylolisthesis			
subjects affected / exposed	0 / 102 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pathological fracture			
subjects affected / exposed	0 / 102 (0.00%)	2 / 268 (0.75%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Bacterial infection			
subjects affected / exposed	0 / 102 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	0 / 102 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium difficile infection			
subjects affected / exposed	0 / 102 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium difficile colitis			
subjects affected / exposed	0 / 102 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	0 / 102 (0.00%)	2 / 268 (0.75%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cystitis			
subjects affected / exposed	0 / 102 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device related infection			

subjects affected / exposed	0 / 102 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulitis			
subjects affected / exposed	0 / 102 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Erysipelas			
subjects affected / exposed	1 / 102 (0.98%)	2 / 268 (0.75%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile infection			
subjects affected / exposed	1 / 102 (0.98%)	0 / 268 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	0 / 102 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes zoster			
subjects affected / exposed	0 / 102 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infection			
subjects affected / exposed	0 / 102 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection			
subjects affected / exposed	0 / 102 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenic sepsis			

subjects affected / exposed	1 / 102 (0.98%)	0 / 268 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	0 / 102 (0.00%)	8 / 268 (2.99%)	
occurrences causally related to treatment / all	0 / 0	1 / 9	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pneumonia pseudomonal			
subjects affected / exposed	0 / 102 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	0 / 102 (0.00%)	3 / 268 (1.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	0 / 102 (0.00%)	3 / 268 (1.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urosepsis			
subjects affected / exposed	0 / 102 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular device infection			
subjects affected / exposed	0 / 102 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound infection			
subjects affected / exposed	0 / 102 (0.00%)	1 / 268 (0.37%)	
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	0 / 102 (0.00%)	5 / 268 (1.87%)	
occurrences causally related to treatment / all	0 / 0	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetes mellitus			
subjects affected / exposed	0 / 102 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Failure to thrive			
subjects affected / exposed	0 / 102 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypercalcaemia			
subjects affected / exposed	0 / 102 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperglycaemia			
subjects affected / exposed	0 / 102 (0.00%)	2 / 268 (0.75%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoglycaemia			
subjects affected / exposed	1 / 102 (0.98%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertriglyceridaemia			
subjects affected / exposed	0 / 102 (0.00%)	1 / 268 (0.37%)	
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 / 102 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyponatraemia			

subjects affected / exposed	0 / 102 (0.00%)	1 / 268 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Investigator Choice (Dacarbazine or Carboplatin+Paclitaxel)	BMS-936558A (Nivolumab)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	97 / 102 (95.10%)	258 / 268 (96.27%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	3 / 102 (2.94%)	21 / 268 (7.84%)	
occurrences (all)	5	61	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	9 / 102 (8.82%)	34 / 268 (12.69%)	
occurrences (all)	21	57	
Fatigue			
subjects affected / exposed	50 / 102 (49.02%)	132 / 268 (49.25%)	
occurrences (all)	78	283	
Chills			
subjects affected / exposed	3 / 102 (2.94%)	18 / 268 (6.72%)	
occurrences (all)	3	27	
Influenza like illness			
subjects affected / exposed	4 / 102 (3.92%)	17 / 268 (6.34%)	
occurrences (all)	6	31	
Pain			
subjects affected / exposed	3 / 102 (2.94%)	27 / 268 (10.07%)	
occurrences (all)	3	39	
Oedema peripheral			
subjects affected / exposed	5 / 102 (4.90%)	39 / 268 (14.55%)	
occurrences (all)	6	53	
Pyrexia			

subjects affected / exposed	9 / 102 (8.82%)	51 / 268 (19.03%)	
occurrences (all)	11	83	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	14 / 102 (13.73%)	50 / 268 (18.66%)	
occurrences (all)	15	69	
Cough			
subjects affected / exposed	7 / 102 (6.86%)	69 / 268 (25.75%)	
occurrences (all)	9	105	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	6 / 102 (5.88%)	33 / 268 (12.31%)	
occurrences (all)	7	40	
Anxiety			
subjects affected / exposed	1 / 102 (0.98%)	19 / 268 (7.09%)	
occurrences (all)	1	23	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	3 / 102 (2.94%)	26 / 268 (9.70%)	
occurrences (all)	4	52	
Blood creatinine increased			
subjects affected / exposed	1 / 102 (0.98%)	19 / 268 (7.09%)	
occurrences (all)	2	44	
Blood alkaline phosphatase increased			
subjects affected / exposed	3 / 102 (2.94%)	21 / 268 (7.84%)	
occurrences (all)	8	33	
Aspartate aminotransferase increased			
subjects affected / exposed	5 / 102 (4.90%)	36 / 268 (13.43%)	
occurrences (all)	6	62	
Neutrophil count decreased			
subjects affected / exposed	8 / 102 (7.84%)	0 / 268 (0.00%)	
occurrences (all)	16	0	
Platelet count decreased			
subjects affected / exposed	9 / 102 (8.82%)	9 / 268 (3.36%)	
occurrences (all)	26	18	
White blood cell count decreased			

subjects affected / exposed	9 / 102 (8.82%)	6 / 268 (2.24%)	
occurrences (all)	28	23	
Weight decreased			
subjects affected / exposed	6 / 102 (5.88%)	23 / 268 (8.58%)	
occurrences (all)	6	34	
Injury, poisoning and procedural complications			
Infusion related reaction			
subjects affected / exposed	9 / 102 (8.82%)	3 / 268 (1.12%)	
occurrences (all)	26	4	
Nervous system disorders			
Dizziness			
subjects affected / exposed	5 / 102 (4.90%)	29 / 268 (10.82%)	
occurrences (all)	6	40	
Headache			
subjects affected / exposed	11 / 102 (10.78%)	43 / 268 (16.04%)	
occurrences (all)	12	68	
Paraesthesia			
subjects affected / exposed	12 / 102 (11.76%)	13 / 268 (4.85%)	
occurrences (all)	12	15	
Neuropathy peripheral			
subjects affected / exposed	11 / 102 (10.78%)	10 / 268 (3.73%)	
occurrences (all)	17	10	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	30 / 102 (29.41%)	60 / 268 (22.39%)	
occurrences (all)	59	160	
Neutropenia			
subjects affected / exposed	23 / 102 (22.55%)	3 / 268 (1.12%)	
occurrences (all)	44	3	
Leukopenia			
subjects affected / exposed	9 / 102 (8.82%)	4 / 268 (1.49%)	
occurrences (all)	19	5	
Thrombocytopenia			
subjects affected / exposed	11 / 102 (10.78%)	8 / 268 (2.99%)	
occurrences (all)	20	13	
Gastrointestinal disorders			

Abdominal pain			
subjects affected / exposed	10 / 102 (9.80%)	49 / 268 (18.28%)	
occurrences (all)	11	77	
Constipation			
subjects affected / exposed	22 / 102 (21.57%)	50 / 268 (18.66%)	
occurrences (all)	27	79	
Abdominal pain upper			
subjects affected / exposed	6 / 102 (5.88%)	21 / 268 (7.84%)	
occurrences (all)	7	30	
Dry mouth			
subjects affected / exposed	2 / 102 (1.96%)	14 / 268 (5.22%)	
occurrences (all)	2	16	
Diarrhoea			
subjects affected / exposed	18 / 102 (17.65%)	84 / 268 (31.34%)	
occurrences (all)	28	210	
Dyspepsia			
subjects affected / exposed	3 / 102 (2.94%)	21 / 268 (7.84%)	
occurrences (all)	5	27	
Nausea			
subjects affected / exposed	42 / 102 (41.18%)	87 / 268 (32.46%)	
occurrences (all)	74	121	
Vomiting			
subjects affected / exposed	24 / 102 (23.53%)	55 / 268 (20.52%)	
occurrences (all)	40	76	
Skin and subcutaneous tissue disorders			
Dry skin			
subjects affected / exposed	2 / 102 (1.96%)	22 / 268 (8.21%)	
occurrences (all)	2	29	
Alopecia			
subjects affected / exposed	29 / 102 (28.43%)	8 / 268 (2.99%)	
occurrences (all)	36	9	
Pruritus			
subjects affected / exposed	2 / 102 (1.96%)	71 / 268 (26.49%)	
occurrences (all)	2	112	
Rash			

subjects affected / exposed	5 / 102 (4.90%)	56 / 268 (20.90%)	
occurrences (all)	6	80	
Rash maculo-papular			
subjects affected / exposed	2 / 102 (1.96%)	21 / 268 (7.84%)	
occurrences (all)	2	48	
Vitiligo			
subjects affected / exposed	0 / 102 (0.00%)	31 / 268 (11.57%)	
occurrences (all)	0	36	
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	0 / 102 (0.00%)	25 / 268 (9.33%)	
occurrences (all)	0	32	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	20 / 102 (19.61%)	74 / 268 (27.61%)	
occurrences (all)	39	151	
Muscle spasms			
subjects affected / exposed	1 / 102 (0.98%)	14 / 268 (5.22%)	
occurrences (all)	1	18	
Back pain			
subjects affected / exposed	0 / 102 (0.00%)	54 / 268 (20.15%)	
occurrences (all)	0	75	
Myalgia			
subjects affected / exposed	10 / 102 (9.80%)	30 / 268 (11.19%)	
occurrences (all)	24	50	
Pain in extremity			
subjects affected / exposed	11 / 102 (10.78%)	36 / 268 (13.43%)	
occurrences (all)	15	50	
Neck pain			
subjects affected / exposed	2 / 102 (1.96%)	15 / 268 (5.60%)	
occurrences (all)	2	16	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	4 / 102 (3.92%)	26 / 268 (9.70%)	
occurrences (all)	5	35	
Upper respiratory tract infection			

subjects affected / exposed	2 / 102 (1.96%)	24 / 268 (8.96%)	
occurrences (all)	2	31	
Urinary tract infection			
subjects affected / exposed	4 / 102 (3.92%)	21 / 268 (7.84%)	
occurrences (all)	4	33	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	20 / 102 (19.61%)	52 / 268 (19.40%)	
occurrences (all)	25	80	
Hypoalbuminaemia			
subjects affected / exposed	0 / 102 (0.00%)	19 / 268 (7.09%)	
occurrences (all)	0	37	
Hyponatraemia			
subjects affected / exposed	1 / 102 (0.98%)	23 / 268 (8.58%)	
occurrences (all)	1	45	
Hypokalaemia			
subjects affected / exposed	1 / 102 (0.98%)	14 / 268 (5.22%)	
occurrences (all)	2	29	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
13 March 2013	Update to Summary of Safety section to include new preliminary reproductive toxicology data that was distributed as a Non-clinical Expedited Safety Report and to include change to the guidance on contraception.
29 April 2013	Modified to expand the number of prior therapies allowed in the eligibility criteria.
24 October 2013	Updated the study design to allow an adequately powered statistical comparison of the co-primary endpoint of Objective Response Rate (ORR) at an earlier timepoint while maintaining the power for statistical comparison of the other co-primary endpoint of Overall Survival (OS).
28 March 2014	Modified the co-primary endpoint to allow a non-comparative estimation of ORR on the nivolumab arm. The OS co-primary endpoint will be tested using 4.9% significance level.
05 October 2016	Modifications to study design and duration. Modifications to Inclusion Criteria. Modifications to treatment duration and dosing calculating. Modification to discontinuation criteria. Modifications to safety assessments.
27 January 2017	Modification to Arm A (Nivolumab) Follow-up assessments.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported