



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. $\geq 50\%$ 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. $\geq 50\%$ 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. $\geq 50\%$ 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 | 11 / 92 (11.96%) | | |
| occurrences (all) | 15 | | |
| Rash | | | |
| subjects affected / exposed | 8 / 92 (8.70%) | | |
| occurrences (all) | 12 | | |
| Skin lesion | | | |
| subjects affected / exposed | 5 / 92 (5.43%) | | |
| occurrences (all) | 6 | | |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 6 / 92 (6.52%) | | |
| occurrences (all) | 10 | | |
| Back pain | | | |
| subjects affected / exposed | 11 / 92 (11.96%) | | |
| occurrences (all) | 12 | | |
| Myalgia | | | |
| subjects affected / exposed | 6 / 92 (6.52%) | | |
| occurrences (all) | 8 | | |
| Muscle spasms | | | |
| subjects affected / exposed | 5 / 92 (5.43%) | | |
| occurrences (all) | 7 | | |
| Infections and infestations | | | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 8 / 92 (8.70%) | | |
| occurrences (all) | 11 | | |
| Pneumonia | | | |
| subjects affected / exposed | 6 / 92 (6.52%) | | |
| occurrences (all) | 7 | | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 11 / 92 (11.96%) | | |
| occurrences (all) | 14 | | |
| Urinary tract infection | | | |

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