



Clinical trial results:

A Phase 2, Fast Real-time Assessment of Combination Therapies in Immuno-ONcology Study in Subjects with Advanced Non-small Cell Lung Cancer (FRACTION-Lung)

Summary

| | |
|--------------------------|-----------------|
| EudraCT number | 2016-001835-11 |
| Trial protocol | ES AT FR IT |
| Global end of trial date | 29 January 2020 |

Results information

| | |
|--------------------------------|------------------|
| Result version number | v1 (current) |
| This version publication date | 12 February 2021 |
| First version publication date | 12 February 2021 |

Trial information

Trial identification

| | |
|-----------------------|-----------|
| Sponsor protocol code | CA018-001 |
|-----------------------|-----------|

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 | 17 March 2020 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 29 January 2020 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

To evaluate the preliminary efficacy, safety, and tolerability of novel FRACTION-Lung treatment combinations in subjects with advanced non-small cell lung cancer (NSCLC).

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 | 06 May 2016 |
| 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 | Austria: 2 |
| Country: Number of subjects enrolled | Australia: 6 |
| Country: Number of subjects enrolled | Canada: 23 |
| Country: Number of subjects enrolled | France: 4 |
| Country: Number of subjects enrolled | Italy: 25 |
| Country: Number of subjects enrolled | Spain: 28 |
| Country: Number of subjects enrolled | Switzerland: 1 |
| Country: Number of subjects enrolled | United States: 206 |
| Worldwide total number of subjects | 295 |
| EEA total number of subjects | 59 |

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) | 149 |
| From 65 to 84 years | 146 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Each of the 295 subjects was assigned to 1 of 5 non-consecutive Tracks (based on previous therapy exposure and/or PD-1/PD-L1 expression). 14 of the 295 subjects, after receiving initial treatment, were re-randomized to a second, different treatment (either under a different Track or within the same Track).

Period 1

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

Arms

| | |
|------------------------------|----|
| Are arms mutually exclusive? | No |
|------------------------------|----|

| | |
|------------------|-----------|
| Arm title | Nivolumab |
|------------------|-----------|

Arm description:

Nivolumab monotherapy 240 mg Q2W administered until completion of 6 cycles (1 cycle=4 weeks)

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

Dosage and administration details:

Flat dose 240 mg Q2W given as an IV over approximately 30 minutes

| | |
|------------------|-----------------------|
| Arm title | Nivolumab + Dasatinib |
|------------------|-----------------------|

Arm description:

Nivolumab 240 mg Q2W + Dasatinib 100 mg QD, administered until completion of 6 cycles (1 cycle=4 weeks)

| | |
|--|--------------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Nivolumab + Dasatinib |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection, Tablet |
| Routes of administration | Intravenous use, Oral use |

Dosage and administration details:

Nivolumab: flat dose 240 mg Q2W Dasatinib: 100 mg QD

| | |
|------------------|-----------------------|
| Arm title | Nivolumab + BMS986016 |
|------------------|-----------------------|

Arm description:

Nivolumab 240 mg Q2W + BMS986016 20 mg Q2W, administered until completion of 6 cycles (1 cycle=4 weeks)

| | |
|----------|--------------|
| Arm type | Experimental |
|----------|--------------|

| | |
|--|------------------------|
| Investigational medicinal product name | Nivolumab + BMS986016 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection |
| Routes of administration | Intravenous use |
| Dosage and administration details: | |
| Nivolumab: flat dose 240 mg Q2W BMS986016: 20 mg Q2W | |
| Arm title | Nivolumab + Ipilimumab |

Arm description:

Nivolumab 240 mg Q2W for 12 doses + Ipilimumab 1 mg/kg Q6W for 4 doses, administered until completion of 24 weeks of study

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

Dosage and administration details:

Nivolumab: flat dose 240 mg Q2W Ipilimumab: 1 mg/Kg Q6W

| | |
|------------------|-----------------------|
| Arm title | Nivolumab + BMS986205 |
|------------------|-----------------------|

Arm description:

Nivolumab 480 mg Q4W + BMS986205 100 mg QD, administered until completion of 6 cycles (1 cycle=4 weeks)

| | |
|--|--------------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Nivolumab + BMS986205 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection, Tablet |
| Routes of administration | Intravenous use, Oral use |

Dosage and administration details:

Nivolumab: flat dose 240 mg Q2W BMS986205: 100 mg QD

| Number of subjects in period 1 | Nivolumab | Nivolumab + Dasatinib | Nivolumab + BMS986016 |
|---------------------------------------|-----------|-----------------------|-----------------------|
| Started | 49 | 104 | 17 |
| Completed | 16 | 9 | 1 |
| Not completed | 33 | 97 | 17 |
| Subject withdrew consent | - | 5 | 1 |
| Disease progression | 24 | 63 | 15 |
| Subject request to discontinue | 1 | 3 | - |
| Study drug toxicity | 5 | 12 | - |
| Death | - | - | - |
| AE unrelated to study drug | 2 | 6 | 1 |
| Other reasons | 1 | 8 | - |
| Joined | 0 | 2 | 1 |

| | | | |
|-------------------------------------|---|---|---|
| Re-randomized to a second treatment | - | 2 | 1 |
|-------------------------------------|---|---|---|

| Number of subjects in period 1 | Nivolumab + Ipilimumab | Nivolumab + BMS986205 |
|---------------------------------------|---------------------------|--------------------------|
| Started | 88 | 37 |
| Completed | 26 | 0 |
| Not completed | 67 | 43 |
| Subject withdrew consent | - | - |
| Disease progression | 52 | 34 |
| Subject request to discontinue | 1 | 3 |
| Study drug toxicity | 9 | 2 |
| Death | 1 | - |
| AE unrelated to study drug | 1 | 2 |
| Other reasons | 3 | 2 |
| Joined | 5 | 6 |
| Re-randomized to a second treatment | 5 | 6 |

Baseline characteristics

Reporting groups^[1]

| | |
|--|------------------------|
| Reporting group title | Nivolumab |
| Reporting group description: Nivolumab monotherapy 240 mg Q2W administered until completion of 6 cycles (1 cycle=4 weeks) | |
| Reporting group title | Nivolumab + Dasatinib |
| Reporting group description: Nivolumab 240 mg Q2W + Dasatinib 100 mg QD, administered until completion of 6 cycles (1 cycle=4 weeks) | |
| Reporting group title | Nivolumab + BMS986016 |
| Reporting group description: Nivolumab 240 mg Q2W + BMS986016 20 mg Q2W, administered until completion of 6 cycles (1 cycle=4 weeks) | |
| Reporting group title | Nivolumab + Ipilimumab |
| Reporting group description: Nivolumab 240 mg Q2W for 12 doses + Ipilimumab 1 mg/kg Q6W for 4 doses, administered until completion of 24 weeks of study | |
| Reporting group title | Nivolumab + BMS986205 |
| Reporting group description: Nivolumab 480 mg Q4W + BMS986205 100 mg QD, administered until completion of 6 cycles (1 cycle=4 weeks) | |

Notes:

[1] - The number of subjects reported to be in the baseline period is not equal to the worldwide number of subjects enrolled in the trial. It is expected that these numbers will be the same.

Justification: 14 subjects, after receiving a first treatment, were re-randomized to a second different treatment group

| Reporting group values | Nivolumab | Nivolumab + Dasatinib | Nivolumab + BMS986016 |
|--|-----------|-----------------------|-----------------------|
| Number of subjects | 49 | 106 | 18 |
| Age categorical Units: Subjects | | | |
| Adults (18-64 years) | 24 | 49 | 8 |
| From 65-84 years | 25 | 57 | 10 |
| Age Continuous Units: Years | | | |
| arithmetic mean | 64.5 | 63.8 | 66.3 |
| standard deviation | ± 10.27 | ± 9.26 | ± 8.99 |
| Sex: Female, Male Units: Participants | | | |
| Female | 21 | 35 | 8 |
| Male | 28 | 71 | 10 |
| Race (NIH/OMB) Units: Subjects | | | |
| Asian | 2 | 7 | 2 |
| Black or African American | 0 | 6 | 1 |
| White | 42 | 87 | 15 |
| Unknown or Not Reported | 5 | 6 | 0 |
| Ethnicity (NIH/OMB) Units: Subjects | | | |
| Hispanic or Latino | 1 | 2 | 0 |
| Not Hispanic or Latino | 25 | 66 | 18 |

| | | | |
|-------------------------|----|----|---|
| Unknown or Not Reported | 23 | 38 | 0 |
|-------------------------|----|----|---|

| Reporting group values | Nivolumab + Ipilimumab | Nivolumab + BMS986205 | Total |
|--|---------------------------|--------------------------|-------|
| Number of subjects | 93 | 43 | 309 |
| Age categorical Units: Subjects | | | |
| Adults (18-64 years) | 51 | 22 | 154 |
| From 65-84 years | 42 | 21 | 155 |
| Age Continuous Units: Years | | | |
| arithmetic mean | 62.4 | 64.5 | |
| standard deviation | ± 8.88 | ± 8.05 | - |
| Sex: Female, Male Units: Participants | | | |
| Female | 39 | 22 | 125 |
| Male | 54 | 21 | 184 |
| Race (NIH/OMB) Units: Subjects | | | |
| Asian | 3 | 4 | 18 |
| Black or African American | 6 | 7 | 20 |
| White | 82 | 30 | 256 |
| Unknown or Not Reported | 2 | 2 | 15 |
| Ethnicity (NIH/OMB) Units: Subjects | | | |
| Hispanic or Latino | 5 | 1 | 9 |
| Not Hispanic or Latino | 63 | 31 | 203 |
| Unknown or Not Reported | 25 | 11 | 97 |

End points

End points reporting groups

| | |
|--|------------------------|
| Reporting group title | Nivolumab |
| Reporting group description: Nivolumab monotherapy 240 mg Q2W administered until completion of 6 cycles (1 cycle=4 weeks) | |
| Reporting group title | Nivolumab + Dasatinib |
| Reporting group description: Nivolumab 240 mg Q2W + Dasatinib 100 mg QD, administered until completion of 6 cycles (1 cycle=4 weeks) | |
| Reporting group title | Nivolumab + BMS986016 |
| Reporting group description: Nivolumab 240 mg Q2W + BMS986016 20 mg Q2W, administered until completion of 6 cycles (1 cycle=4 weeks) | |
| Reporting group title | Nivolumab + Ipilimumab |
| Reporting group description: Nivolumab 240 mg Q2W for 12 doses + Ipilimumab 1 mg/kg Q6W for 4 doses, administered until completion of 24 weeks of study | |
| Reporting group title | Nivolumab + BMS986205 |
| Reporting group description: Nivolumab 480 mg Q4W + BMS986205 100 mg QD, administered until completion of 6 cycles (1 cycle=4 weeks) | |

Primary: Objective Response Rate (ORR)

| | |
|--|--|
| End point title | Objective Response Rate (ORR) ^[1] |
| End point description: ORR is defined as the percentage of subjects whose confirmed best overall response (BOR) is either a complete response (CR) or partial response (PR). BOR was assessed by investigator per RECIST1.1. Results are presented by study tracks. IO YES/NO = Prior immuno-oncology therapy exposure status. PD-L1 + = PD-L1 expression levels ≥1%. PD-L1 - = PD-L1 expression levels <1%. Results for treatment groups not receiving treatment during a specific study track are indicated as 99999. | |
| End point type | Primary |
| End point timeframe: From first dose to 2 years following last dose (up to 30 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: ORR is estimated and corresponding exact two-sided 95% CI is derived based Clopper and Pearson method.

| End point values | Nivolumab | Nivolumab + Dasatinib | Nivolumab + BMS986016 | Nivolumab + Ipilimumab |
|----------------------------------|------------------------|-----------------------|------------------------|------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 49 ^[2] | 106 ^[3] | 18 ^[4] | 93 ^[5] |
| Units: Percent of Subjects | | | | |
| number (confidence interval 95%) | | | | |
| Track 1 = NO IO - PD-L1 + | 17.5 (7.3 to 32.8) | 25.0 (0.6 to 80.6) | 99999 (99999 to 99999) | 0 (0.0 to 70.8) |
| Track 2 = NO IO - PD-L1 - | 0 (0.0 to 33.6) | 0 (0.0 to 33.6) | 0 (0.0 to 84.2) | 25.0 (5.5 to 57.2) |
| Track 3 = YES IO | 99999 (99999 to 99999) | 2.4 (0.1 to 12.9) | 0 (0.0 to 20.6) | 5.6 (0.1 to 27.3) |

| | | | | |
|---|------------------------|------------------------|------------------------|------------------------|
| Track 4 = NO IO (after enrollment stop in 1,2,3) | 99999 (99999 to 99999) | 1.9 (0.0 to 10.1) | 99999 (99999 to 99999) | 20.0 (10.8 to 32.3) |
| Track 5 = YES IO (after enrollment stop in 1,2,3) | 99999 (99999 to 99999) | 99999 (99999 to 99999) | 99999 (99999 to 99999) | 99999 (99999 to 99999) |

Notes:

[2] - Track1=40 Track2=9 Track3=0 Track4=0 Track5=0

[3] - Track1=4 Track2=8 Track3=41 Track4=53 Track5=0

[4] - Track1=0 Track2=2 Track3=16 Track4=0 Track5=0

[5] - Track1=3 Track2=12 Track3=18 Track4=60 Track5=0

| | | | | |
|---|------------------------|--|--|--|
| End point values | Nivolumab + BMS986205 | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 43 ^[6] | | | |
| Units: Percent of Subjects | | | | |
| number (confidence interval 95%) | | | | |
| Track 1 = NO IO - PD-L1 + | 9999 (9999 to 9999) | | | |
| Track 2 = NO IO - PD-L1 - | 99999 (99999 to 99999) | | | |
| Track 3 = YES IO | 99999 (99999 to 99999) | | | |
| Track 4 = NO IO (after enrollment stop in 1,2,3) | 99999 (99999 to 99999) | | | |
| Track 5 = YES IO (after enrollment stop in 1,2,3) | 2.3 (0.1 to 12.3) | | | |

Notes:

[6] - Track1=0 Track2=0 Track3=0 Track4=0 Track5=43

Statistical analyses

No statistical analyses for this end point

Primary: Duration of Response (DOR)

| | |
|--|---|
| End point title | Duration of Response (DOR) ^[7] |
| End point description: | |
| DOR, computed for all treated subjects with a confirmed BOR of CR or PR, is defined as the time between the date of first response and the date of first documented disease progression (as determined by RECIST 1.1) or death due to any cause. Results are presented by study tracks. IO YES/NO = Prior immuno-oncology therapy exposure status. PD-L1 + = PD-L1 expression levels $\geq 1\%$. PD-L1 - = PD-L1 expression levels $< 1\%$. Results for treatment groups not receiving treatment during a specific study track or for which a value was not calculable are indicated as 99999. | |
| End point type | Primary |

End point timeframe:

From first dose to 2 years following last dose (up to 30 months)

Notes:

[7] - 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: DOR is estimated using the Kaplan-Meier (KM) product limit method. Median values of DOR, along with two-sided 95% CI, is computed based on a log-log transformation method.

| End point values | Nivolumab | Nivolumab + Dasatinib | Nivolumab + BMS986016 | Nivolumab + Ipilimumab |
|---|------------------------|------------------------|-----------------------|------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 7 ^[8] | 3 ^[9] | 0 ^[10] | 16 ^[11] |
| Units: Months | | | | |
| median (confidence interval 95%) | | | | |
| Track 1 = NO IO - PD-L1 + | 12.81 (0.03 to 99999) | 8.57 (-99999 to 99999) | (to) | 99999 (99999 to 99999) |
| Track 2 = NO IO - PD-L1 - | 99999 (99999 to 99999) | 99999 (99999 to 99999) | (to) | 99999 (99999 to 99999) |
| Track 3 = YES IO | 99999 (99999 to 99999) | 99999 (99999 to 99999) | (to) | 99999 (99999 to 99999) |
| Track 4 = NO IO (after enrollment stop in 1,2,3) | 99999 (99999 to 99999) | 99999 (99999 to 99999) | (to) | 12.65 (8.77 to 99999) |
| Track 5 = YES IO (after enrollment stop in 1,2,3) | 99999 (99999 to 99999) | 99999 (99999 to 99999) | (to) | 99999 (99999 to 99999) |

Notes:

[8] - Track1=7

Track2=0

Track3=0

Track4=0

Track5=0

[9] - Track1=1

Track2=0

Track3=1

Track4=1

Track5=0

[10] - Track1=0

Track2=0

Track3=0

Track4=0

Track5=0

[11] - Track1=0

Track2=3

Track3=1

Track4=12

Track5=0

| End point values | Nivolumab + BMS986205 | | | |
|---|------------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 1 ^[12] | | | |
| Units: Months | | | | |
| median (confidence interval 95%) | | | | |
| Track 1 = NO IO - PD-L1 + | 99999 (99999 to 99999) | | | |
| Track 2 = NO IO - PD-L1 - | 99999 (99999 to 99999) | | | |
| Track 3 = YES IO | 99999 (99999 to 99999) | | | |
| Track 4 = NO IO (after enrollment stop in 1,2,3) | 99999 (99999 to 99999) | | | |
| Track 5 = YES IO (after enrollment stop in 1,2,3) | 3.75 (-99999 to 99999) | | | |

Notes:

[12] - Track1=0

Track2=0

Track3=0

Track4=0

Track5=1

Statistical analyses

Primary: Progression Free Survival Rate (PFSR) at 24 Weeks

| | |
|-----------------|---|
| End point title | Progression Free Survival Rate (PFSR) at 24 Weeks ^[13] |
|-----------------|---|

End point description:

The PFSR at 24 weeks is defined as the proportion of treated subjects remaining progression free and surviving at 24 weeks since the first dosing date. Results are presented by study tracks and only for the treatment groups with a sufficient number of subjects remaining progression-free during the timeframe ($n \geq 5$). IO YES/NO = Prior immuno-oncology therapy exposure status. PD-L1 + = PD-L1 expression levels $\geq 1\%$. PD-L1 - = PD-L1 expression levels $< 1\%$. Results for treatment groups not receiving treatment during a specific study track or with an insufficient number of subjects remaining progression-free are indicated as 99999.

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

From first dose to 24 weeks after first dose

Notes:

[13] - 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: PFSR at 24 weeks is derived from the Kaplan Meier estimate and corresponding CIs are derived based on Greenwood formula for variance derivation and on log-log transformation applied on the survivor function.

| End point values | Nivolumab | Nivolumab + Dasatinib | Nivolumab + BMS986016 | Nivolumab + Ipilimumab |
|---|------------------------|------------------------|------------------------|------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 49 ^[14] | 106 ^[15] | 18 ^[16] | 93 ^[17] |
| Units: Proportion of Participants | | | | |
| number (confidence interval 95%) | | | | |
| Track 1 = NO IO - PD-L1 + | 0.302 (0.164 to 0.451) | 99999 (99999 to 99999) | 99999 (99999 to 99999) | 99999 (99999 to 99999) |
| Track 2 = NO IO - PD-L1 - | 99999 (99999 to 99999) | 99999 (99999 to 99999) | 99999 (99999 to 99999) | 0.455 (0.167 to 0.707) |
| Track 3 = YES IO | 99999 (99999 to 99999) | 0.191 (0.079 to 0.340) | 99999 (99999 to 99999) | 99999 (99999 to 99999) |
| Track 4 = NO IO (after enrollment stop in 1,2,3) | 99999 (99999 to 99999) | 99999 (99999 to 99999) | 99999 (99999 to 99999) | 0.391 (0.265 to 0.514) |
| Track 5 = YES IO (after enrollment stop in 1,2,3) | 99999 (99999 to 99999) | 99999 (99999 to 99999) | 99999 (99999 to 99999) | 99999 (99999 to 99999) |

Notes:

[14] - Track1=40 Track2=9 Track3=0 Track4=0 Track5=0

[15] - Track1=4 Track2=8 Track3=41 Track4=53 Track5=0

[16] - Track1=0 Track2=2 Track3=16 Track4=0 Track5=0

[17] - Track1=3 Track2=12 Track3=18 Track4=60 Track5=0

| End point values | Nivolumab + BMS986205 | | | |
|--|------------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 43 ^[18] | | | |
| Units: Proportion of Participants | | | | |
| number (confidence interval 95%) | | | | |
| Track 1 = NO IO - PD-L1 + | 99999 (99999 to 99999) | | | |
| Track 2 = NO IO - PD-L1 - | 99999 (99999 to 99999) | | | |
| Track 3 = YES IO | 99999 (99999 to 99999) | | | |
| Track 4 = NO IO (after enrollment stop in 1,2,3) | 99999 (99999 to 99999) | | | |

| | | | | |
|---|------------------------|--|--|--|
| Track 5 = YES IO (after enrollment stop in 1,2,3) | 0.111 (0.036 to 0.235) | | | |
|---|------------------------|--|--|--|

Notes:

[18] - Track1=0 Track2=0 Track3=0 Track4=0 Track5=43

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Experiencing Adverse Events (AEs)

| | |
|-----------------|--|
| End point title | Percentage of Subjects Experiencing Adverse Events (AEs) |
|-----------------|--|

End point description:

This outcome measure describes the percentage of subjects who experienced any grade, all causality AEs during the specified time frame

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

From first dose to 100 days following last dose

| End point values | Nivolumab | Nivolumab + Dasatinib | Nivolumab + BMS986016 | Nivolumab + Ipilimumab |
|-----------------------------|-----------------|-----------------------|-----------------------|------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 49 | 106 | 18 | 93 |
| Units: Percent of Subjects | | | | |
| number (not applicable) | 100.0 | 100.0 | 100.0 | 98.9 |

| End point values | Nivolumab + BMS986205 | | | |
|-----------------------------|-----------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 43 | | | |
| Units: Percent of Subjects | | | | |
| number (not applicable) | 100.0 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Experiencing Serious Adverse Events (SAEs)

| | |
|-----------------|---|
| End point title | Percentage of Subjects Experiencing Serious Adverse Events (SAEs) |
|-----------------|---|

End point description:

This outcome measure describes the percentage of subjects who experienced any grade, all causality SAEs during the specified time frame

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

From first dose to 100 days following last dose

| End point values | Nivolumab | Nivolumab + Dasatinib | Nivolumab + BMS986016 | Nivolumab + Ipilimumab |
|-----------------------------|-----------------|-----------------------|-----------------------|------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 49 | 106 | 18 | 93 |
| Units: Percent of Subjects | | | | |
| number (not applicable) | 57.1 | 53.8 | 61.1 | 58.1 |

| End point values | Nivolumab + BMS986205 | | | |
|-----------------------------|-----------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 43 | | | |
| Units: Percent of Subjects | | | | |
| number (not applicable) | 60.5 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Experiencing Adverse Events (AEs) Leading to Discontinuation

| | |
|-----------------|---|
| End point title | Percentage of Subjects Experiencing Adverse Events (AEs) Leading to Discontinuation |
|-----------------|---|

End point description:

This outcome measure describes the percentage of subjects who experienced all causality AEs leading to discontinuation of study therapy during the specified time frame

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

From first dose to 100 days following last dose

| End point values | Nivolumab | Nivolumab + Dasatinib | Nivolumab + BMS986016 | Nivolumab + Ipilimumab |
|-----------------------------|-----------------|-----------------------|-----------------------|------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 49 | 106 | 18 | 93 |
| Units: Percent of Subjects | | | | |
| number (not applicable) | 14.3 | 23.6 | 5.6 | 11.8 |

| End point values | Nivolumab + | | | |
|------------------|-------------|--|--|--|
|------------------|-------------|--|--|--|

| | | | | |
|-----------------------------|-----------------|--|--|--|
| | BMS986205 | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 43 | | | |
| Units: Percent of Subjects | | | | |
| number (not applicable) | 14.0 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Experiencing Death

| | |
|---|---|
| End point title | Percentage of Subjects Experiencing Death |
| End point description: This outcome measure describes the percentage of subjects who died (due to any cause) during the specified time frame | |
| End point type | Secondary |
| End point timeframe: From first dose to up to 45 months following first dose | |

| End point values | Nivolumab | Nivolumab + Dasatinib | Nivolumab + BMS986016 | Nivolumab + Ipilimumab |
|-----------------------------|-----------------|-----------------------|-----------------------|------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 49 | 106 | 18 | 93 |
| Units: Percent of Subjects | | | | |
| number (not applicable) | 57.1 | 55.7 | 66.7 | 46.2 |

| End point values | Nivolumab + BMS986205 | | | |
|-----------------------------|-----------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 43 | | | |
| Units: Percent of Subjects | | | | |
| number (not applicable) | 62.8 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects Experiencing Laboratory Abnormalities in Hepatic Tests

| | |
|-----------------|---|
| End point title | Number of Subjects Experiencing Laboratory Abnormalities in Hepatic Tests |
|-----------------|---|

End point description:

The following measurements will be considered laboratory abnormalities for hepatic tests: - ALT or AST > 3 x ULN, > 5 x ULN, > 10 x ULN and > 20 x ULN - Total bilirubin > 2 x ULN - Concurrent (within 1 day) ALT or AST > 3 x ULN and total bilirubin > 2 x ULN - Concurrent (within 30 days) ALT or AST > 3 x ULN and total bilirubin > 2 x ULN ALT=Alanine aminotransferase AST=Aspartate aminotransferase ULN=Upper Limit of Normal

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

From first dose to 100 days following last dose

| End point values | Nivolumab | Nivolumab + Dasatinib | Nivolumab + BMS986016 | Nivolumab + Ipilimumab |
|--|-----------------|-----------------------|-----------------------|------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 49 | 106 | 18 | 93 |
| Units: Subjects | | | | |
| ALT OR AST > 3XULN | 4 | 3 | 1 | 5 |
| ALT OR AST > 5XULN | 2 | 0 | 0 | 3 |
| ALT OR AST > 10XULN | 2 | 0 | 0 | 1 |
| ALT OR AST > 20XULN | 0 | 0 | 0 | 1 |
| TOTAL BILIRUBIN > 2XULN | 1 | 0 | 0 | 2 |
| (1 day) ALT or AST>3x ULN and total bilir.>2x ULN | 0 | 0 | 0 | 2 |
| (30 day) ALT or AST>3x ULN and total bilir.>2x ULN | 0 | 0 | 0 | 2 |

| End point values | Nivolumab + BMS986205 | | | |
|--|-----------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 43 | | | |
| Units: Subjects | | | | |
| ALT OR AST > 3XULN | 3 | | | |
| ALT OR AST > 5XULN | 2 | | | |
| ALT OR AST > 10XULN | 2 | | | |
| ALT OR AST > 20XULN | 1 | | | |
| TOTAL BILIRUBIN > 2XULN | 3 | | | |
| (1 day) ALT or AST>3x ULN and total bilir.>2x ULN | 2 | | | |
| (30 day) ALT or AST>3x ULN and total bilir.>2x ULN | 2 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects Experiencing Laboratory Abnormalities in Thyroid Tests

| | |
|-----------------|---|
| End point title | Number of Subjects Experiencing Laboratory Abnormalities in |
|-----------------|---|

End point description:

The following measurements will be considered laboratory abnormalities for thyroid tests:

- TSH value > ULN and
 - With baseline TSH value \leq ULN
 - At least one T3/T4 test value < LLN
- Low TSH < LLN and
 - With baseline TSH value \geq LLN
 - At least one T3/T4 test value > ULN

TSH = thyroid stimulating hormone

ULN=Upper Limit of Normal

LLN=Lower Limit of Normal

T3=Triiodothyronine

T4=Thyroxin

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

From first dose to 100 days following last dose

| End point values | Nivolumab | Nivolumab + Dasatinib | Nivolumab + BMS986016 | Nivolumab + Ipilimumab |
|---|-----------------|-----------------------|-----------------------|------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 29 | 76 | 14 | 75 |
| Units: Subjects | | | | |
| TSH > ULN | 9 | 16 | 3 | 24 |
| TSH > ULN WITH TSH \leq ULN AT BASELINE | 6 | 9 | 1 | 17 |
| TSH > ULN AT LEAST 1 FT3/FT4 VALUE < LLN | 4 | 3 | 1 | 8 |
| TSH < LLN | 5 | 3 | 0 | 20 |
| TSH < LLN WITH TSH \geq LLN AT BASELINE | 5 | 1 | 0 | 16 |
| TSH < LLN AT LEAST 1 FT3/FT4 VALUE > ULN | 3 | 1 | 0 | 5 |

| End point values | Nivolumab + BMS986205 | | | |
|---|-----------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 35 | | | |
| Units: Subjects | | | | |
| TSH > ULN | 9 | | | |
| TSH > ULN WITH TSH \leq ULN AT BASELINE | 6 | | | |
| TSH > ULN AT LEAST 1 FT3/FT4 VALUE < LLN | 6 | | | |
| TSH < LLN | 4 | | | |
| TSH < LLN WITH TSH \geq LLN AT BASELINE | 4 | | | |
| TSH < LLN AT LEAST 1 FT3/FT4 VALUE > ULN | 0 | | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Deaths = collected from first dose to up to 45 months following first dose

Serious adverse events and other adverse events = collected from start of treatment up to 100 days of discontinuation of dosing.

| | |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

Dictionary used

| | |
|--------------------|--------|
| Dictionary name | MedDRA |
| Dictionary version | 22.1 |

Reporting groups

| | |
|-----------------------|-----------|
| Reporting group title | Nivolumab |
|-----------------------|-----------|

Reporting group description:

Nivolumab monotherapy 240 mg Q2W administered until completion of 6 cycles (1 cycle=4 weeks)

| | |
|-----------------------|-----------------------|
| Reporting group title | Nivolumab + Dasatinib |
|-----------------------|-----------------------|

Reporting group description:

Nivolumab 240 mg Q2W + Dasatinib 100 mg QD, administered until completion of 6 cycles (1 cycle=4 weeks)

| | |
|-----------------------|-----------------------|
| Reporting group title | Nivolumab + BMS986016 |
|-----------------------|-----------------------|

Reporting group description:

Nivolumab 240 mg Q2W + BMS986016 20 mg Q2W, administered until completion of 6 cycles (1 cycle=4 weeks)

| | |
|-----------------------|------------------------|
| Reporting group title | Nivolumab + Ipilimumab |
|-----------------------|------------------------|

Reporting group description:

Nivolumab 240 mg Q2W for 12 doses + Ipilimumab 1 mg/kg Q6W for 4 doses, administered until completion of 24 weeks of study

| | |
|-----------------------|-----------------------|
| Reporting group title | Nivolumab + BMS986205 |
|-----------------------|-----------------------|

Reporting group description:

Nivolumab 480 mg Q4W + BMS986205 100 mg QD, administered until completion of 6 cycles (1 cycle=4 weeks)

| Serious adverse events | Nivolumab | Nivolumab + Dasatinib | Nivolumab + BMS986016 |
|---|------------------|-----------------------|-----------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 28 / 49 (57.14%) | 57 / 106 (53.77%) | 11 / 18 (61.11%) |
| number of deaths (all causes) | 28 | 59 | 12 |
| number of deaths resulting from adverse events | | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Basal cell carcinoma | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 0 / 106 (0.00%) | 0 / 18 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cancer pain | | | |

| | | | |
|---|------------------|-------------------|-----------------|
| subjects affected / exposed | 0 / 49 (0.00%) | 1 / 106 (0.94%) | 0 / 18 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lung neoplasm malignant | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 1 / 106 (0.94%) | 0 / 18 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| Malignant neoplasm progression | | | |
| subjects affected / exposed | 12 / 49 (24.49%) | 29 / 106 (27.36%) | 4 / 18 (22.22%) |
| occurrences causally related to treatment / all | 0 / 12 | 0 / 30 | 0 / 4 |
| deaths causally related to treatment / all | 0 / 11 | 0 / 27 | 0 / 4 |
| Malignant pleural effusion | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 0 / 106 (0.00%) | 0 / 18 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metastases to meninges | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 0 / 106 (0.00%) | 0 / 18 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Neoplasm progression | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 0 / 106 (0.00%) | 0 / 18 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Second primary malignancy | | | |
| subjects affected / exposed | 1 / 49 (2.04%) | 0 / 106 (0.00%) | 0 / 18 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| Tumour pain | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 0 / 106 (0.00%) | 1 / 18 (5.56%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vascular disorders | | | |
| Deep vein thrombosis | | | |

| | | | |
|--|----------------|-----------------|----------------|
| subjects affected / exposed | 0 / 49 (0.00%) | 0 / 106 (0.00%) | 0 / 18 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypotension | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 1 / 106 (0.94%) | 0 / 18 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Orthostatic hypotension | | | |
| subjects affected / exposed | 1 / 49 (2.04%) | 0 / 106 (0.00%) | 0 / 18 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Superior vena cava syndrome | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 0 / 106 (0.00%) | 1 / 18 (5.56%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General disorders and administration site conditions | | | |
| Euthanasia | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 1 / 106 (0.94%) | 0 / 18 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| Fatigue | | | |
| subjects affected / exposed | 1 / 49 (2.04%) | 2 / 106 (1.89%) | 0 / 18 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 2 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General physical health deterioration | | | |
| subjects affected / exposed | 1 / 49 (2.04%) | 0 / 106 (0.00%) | 0 / 18 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Influenza like illness | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 0 / 106 (0.00%) | 0 / 18 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Oedema peripheral | | | |

| | | | |
|---|----------------|-----------------|----------------|
| subjects affected / exposed | 1 / 49 (2.04%) | 0 / 106 (0.00%) | 0 / 18 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pain | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 1 / 106 (0.94%) | 0 / 18 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pyrexia | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 3 / 106 (2.83%) | 0 / 18 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 3 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| Reproductive system and breast disorders | | | |
| Scrotal oedema | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 1 / 106 (0.94%) | 0 / 18 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Acute respiratory failure | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 1 / 106 (0.94%) | 0 / 18 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| Atelectasis | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 0 / 106 (0.00%) | 0 / 18 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bronchial obstruction | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 0 / 106 (0.00%) | 0 / 18 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Chronic obstructive pulmonary disease | | | |

| | | | |
|---|----------------|-----------------|----------------|
| subjects affected / exposed | 2 / 49 (4.08%) | 0 / 106 (0.00%) | 1 / 18 (5.56%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| Dyspnoea | | | |
| subjects affected / exposed | 2 / 49 (4.08%) | 7 / 106 (6.60%) | 0 / 18 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 8 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Haemoptysis | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 2 / 106 (1.89%) | 0 / 18 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypoxia | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 2 / 106 (1.89%) | 0 / 18 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Interstitial lung disease | | | |
| subjects affected / exposed | 1 / 49 (2.04%) | 0 / 106 (0.00%) | 0 / 18 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lung consolidation | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 0 / 106 (0.00%) | 0 / 18 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Oesophagobronchial fistula | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 0 / 106 (0.00%) | 0 / 18 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pleural effusion | | | |
| subjects affected / exposed | 2 / 49 (4.08%) | 7 / 106 (6.60%) | 0 / 18 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 3 / 7 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| Pneumonitis | | | |

| | | | |
|---|----------------|-----------------|----------------|
| subjects affected / exposed | 3 / 49 (6.12%) | 6 / 106 (5.66%) | 1 / 18 (5.56%) |
| occurrences causally related to treatment / all | 3 / 3 | 6 / 8 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| Pneumothorax | | | |
| subjects affected / exposed | 1 / 49 (2.04%) | 1 / 106 (0.94%) | 0 / 18 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary embolism | | | |
| subjects affected / exposed | 4 / 49 (8.16%) | 0 / 106 (0.00%) | 1 / 18 (5.56%) |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory distress | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 1 / 106 (0.94%) | 0 / 18 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory failure | | | |
| subjects affected / exposed | 1 / 49 (2.04%) | 2 / 106 (1.89%) | 0 / 18 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| Psychiatric disorders | | | |
| Confusional state | | | |
| subjects affected / exposed | 2 / 49 (4.08%) | 1 / 106 (0.94%) | 0 / 18 (0.00%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Delirium | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 1 / 106 (0.94%) | 0 / 18 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Mental status changes | | | |
| subjects affected / exposed | 1 / 49 (2.04%) | 1 / 106 (0.94%) | 0 / 18 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Investigations | | | |

| | | | |
|---|----------------|-----------------|----------------|
| Blood bilirubin increased | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 0 / 106 (0.00%) | 0 / 18 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood creatine phosphokinase increased | | | |
| subjects affected / exposed | 1 / 49 (2.04%) | 0 / 106 (0.00%) | 0 / 18 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Human chorionic gonadotropin positive | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 0 / 106 (0.00%) | 0 / 18 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Transaminases increased | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 0 / 106 (0.00%) | 0 / 18 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Injury, poisoning and procedural complications | | | |
| Ankle fracture | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 1 / 106 (0.94%) | 0 / 18 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Fall | | | |
| subjects affected / exposed | 1 / 49 (2.04%) | 0 / 106 (0.00%) | 0 / 18 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Humerus fracture | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 1 / 106 (0.94%) | 0 / 18 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infusion related reaction | | | |

| | | | |
|---|----------------|-----------------|----------------|
| subjects affected / exposed | 0 / 49 (0.00%) | 1 / 106 (0.94%) | 0 / 18 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Overdose | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 1 / 106 (0.94%) | 0 / 18 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Subdural haematoma | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 0 / 106 (0.00%) | 0 / 18 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Toxicity to various agents | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 0 / 106 (0.00%) | 0 / 18 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac disorders | | | |
| Atrial fibrillation | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 1 / 106 (0.94%) | 0 / 18 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Atrial flutter | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 0 / 106 (0.00%) | 1 / 18 (5.56%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac arrest | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 1 / 106 (0.94%) | 0 / 18 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac tamponade | | | |
| subjects affected / exposed | 1 / 49 (2.04%) | 0 / 106 (0.00%) | 0 / 18 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Myocarditis | | | |

| | | | |
|---|----------------|-----------------|----------------|
| subjects affected / exposed | 1 / 49 (2.04%) | 0 / 106 (0.00%) | 0 / 18 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pericardial effusion | | | |
| subjects affected / exposed | 3 / 49 (6.12%) | 1 / 106 (0.94%) | 0 / 18 (0.00%) |
| occurrences causally related to treatment / all | 0 / 3 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Supraventricular tachycardia | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 0 / 106 (0.00%) | 0 / 18 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Tachycardia | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 0 / 106 (0.00%) | 0 / 18 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| Brachial plexopathy | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 1 / 106 (0.94%) | 0 / 18 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cerebral ischaemia | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 0 / 106 (0.00%) | 0 / 18 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cerebrovascular accident | | | |
| subjects affected / exposed | 1 / 49 (2.04%) | 1 / 106 (0.94%) | 1 / 18 (5.56%) |
| occurrences causally related to treatment / all | 0 / 2 | 1 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| Dizziness | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 1 / 106 (0.94%) | 0 / 18 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Facial paralysis | | | |

| | | | |
|---|----------------|-----------------|----------------|
| subjects affected / exposed | 0 / 49 (0.00%) | 0 / 106 (0.00%) | 0 / 18 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Haemorrhage intracranial | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 1 / 106 (0.94%) | 0 / 18 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Headache | | | |
| subjects affected / exposed | 1 / 49 (2.04%) | 0 / 106 (0.00%) | 0 / 18 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ischaemic stroke | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 0 / 106 (0.00%) | 1 / 18 (5.56%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Peripheral sensory neuropathy | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 0 / 106 (0.00%) | 0 / 18 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Polyneuropathy | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 0 / 106 (0.00%) | 0 / 18 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Seizure | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 1 / 106 (0.94%) | 0 / 18 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Spinal cord compression | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 0 / 106 (0.00%) | 0 / 18 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood and lymphatic system disorders | | | |
| Neutropenia | | | |

| | | | |
|---|----------------|-----------------|----------------|
| subjects affected / exposed | 0 / 49 (0.00%) | 0 / 106 (0.00%) | 0 / 18 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Eye disorders | | | |
| Vision blurred | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 0 / 106 (0.00%) | 0 / 18 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Visual impairment | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 0 / 106 (0.00%) | 0 / 18 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 0 / 106 (0.00%) | 0 / 18 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Colitis | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 2 / 106 (1.89%) | 0 / 18 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 3 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Constipation | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 0 / 106 (0.00%) | 0 / 18 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diarrhoea | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 1 / 106 (0.94%) | 0 / 18 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Large intestinal obstruction | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 0 / 106 (0.00%) | 1 / 18 (5.56%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nausea | | | |

| | | | |
|---|----------------|-----------------|----------------|
| subjects affected / exposed | 0 / 49 (0.00%) | 3 / 106 (2.83%) | 0 / 18 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 3 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Oesophageal food impaction | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 1 / 106 (0.94%) | 0 / 18 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Peritoneal haemorrhage | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 0 / 106 (0.00%) | 0 / 18 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vomiting | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 1 / 106 (0.94%) | 0 / 18 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatobiliary disorders | | | |
| Cholecystitis acute | | | |
| subjects affected / exposed | 1 / 49 (2.04%) | 0 / 106 (0.00%) | 0 / 18 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatitis | | | |
| subjects affected / exposed | 2 / 49 (4.08%) | 0 / 106 (0.00%) | 0 / 18 (0.00%) |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hyperbilirubinaemia | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 0 / 106 (0.00%) | 0 / 18 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Skin and subcutaneous tissue disorders | | | |
| Stevens-Johnson syndrome | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 0 / 106 (0.00%) | 0 / 18 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal and urinary disorders | | | |

| | | | |
|---|----------------|-----------------|----------------|
| Acute kidney injury | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 1 / 106 (0.94%) | 0 / 18 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Endocrine disorders | | | |
| Adrenal insufficiency | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 1 / 106 (0.94%) | 0 / 18 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypoparathyroidism | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 0 / 106 (0.00%) | 0 / 18 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypophysitis | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 0 / 106 (0.00%) | 0 / 18 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 2 / 49 (4.08%) | 0 / 106 (0.00%) | 0 / 18 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Back pain | | | |
| subjects affected / exposed | 1 / 49 (2.04%) | 0 / 106 (0.00%) | 0 / 18 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Flank pain | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 0 / 106 (0.00%) | 0 / 18 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Muscular weakness | | | |
| subjects affected / exposed | 1 / 49 (2.04%) | 0 / 106 (0.00%) | 0 / 18 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|----------------|-----------------|----------------|
| Musculoskeletal chest pain | | | |
| subjects affected / exposed | 1 / 49 (2.04%) | 0 / 106 (0.00%) | 0 / 18 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Osteolysis | | | |
| subjects affected / exposed | 1 / 49 (2.04%) | 0 / 106 (0.00%) | 0 / 18 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pain in extremity | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 0 / 106 (0.00%) | 0 / 18 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Sjogren's syndrome | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 0 / 106 (0.00%) | 0 / 18 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Appendicitis | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 0 / 106 (0.00%) | 0 / 18 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Brain abscess | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 1 / 106 (0.94%) | 0 / 18 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Clostridium difficile colitis | | | |
| subjects affected / exposed | 1 / 49 (2.04%) | 0 / 106 (0.00%) | 0 / 18 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Enterocolitis infectious | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 0 / 106 (0.00%) | 1 / 18 (5.56%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Influenza | | | |

| | | | |
|---|----------------|-----------------|----------------|
| subjects affected / exposed | 0 / 49 (0.00%) | 0 / 106 (0.00%) | 0 / 18 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pharyngitis streptococcal | | | |
| subjects affected / exposed | 1 / 49 (2.04%) | 0 / 106 (0.00%) | 0 / 18 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia | | | |
| subjects affected / exposed | 3 / 49 (6.12%) | 2 / 106 (1.89%) | 0 / 18 (0.00%) |
| occurrences causally related to treatment / all | 0 / 3 | 2 / 3 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia bacterial | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 0 / 106 (0.00%) | 0 / 18 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Post procedural infection | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 1 / 106 (0.94%) | 0 / 18 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory tract infection | | | |
| subjects affected / exposed | 1 / 49 (2.04%) | 1 / 106 (0.94%) | 0 / 18 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| Sepsis | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 1 / 106 (0.94%) | 1 / 18 (5.56%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| Septic shock | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 2 / 106 (1.89%) | 0 / 18 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Staphylococcal infection | | | |

| | | | |
|---|----------------|-----------------|----------------|
| subjects affected / exposed | 0 / 49 (0.00%) | 0 / 106 (0.00%) | 0 / 18 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urinary tract infection | | | |
| subjects affected / exposed | 1 / 49 (2.04%) | 0 / 106 (0.00%) | 0 / 18 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metabolism and nutrition disorders | | | |
| Dehydration | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 0 / 106 (0.00%) | 1 / 18 (5.56%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diabetes mellitus | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 0 / 106 (0.00%) | 0 / 18 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diabetic ketoacidosis | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 0 / 106 (0.00%) | 0 / 18 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Failure to thrive | | | |
| subjects affected / exposed | 1 / 49 (2.04%) | 1 / 106 (0.94%) | 1 / 18 (5.56%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypercalcaemia | | | |
| subjects affected / exposed | 1 / 49 (2.04%) | 2 / 106 (1.89%) | 0 / 18 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hyperglycaemia | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 0 / 106 (0.00%) | 0 / 18 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hyponatraemia | | | |

| | | | |
|---|----------------|-----------------|----------------|
| subjects affected / exposed | 0 / 49 (0.00%) | 2 / 106 (1.89%) | 0 / 18 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| Serious adverse events | Nivolumab + Ipilimumab | Nivolumab + BMS986205 | |
|---|---------------------------|--------------------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 54 / 93 (58.06%) | 26 / 43 (60.47%) | |
| number of deaths (all causes) | 43 | 27 | |
| number of deaths resulting from adverse events | | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Basal cell carcinoma | | | |
| subjects affected / exposed | 1 / 93 (1.08%) | 0 / 43 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cancer pain | | | |
| subjects affected / exposed | 0 / 93 (0.00%) | 0 / 43 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lung neoplasm malignant | | | |
| subjects affected / exposed | 0 / 93 (0.00%) | 0 / 43 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Malignant neoplasm progression | | | |
| subjects affected / exposed | 20 / 93 (21.51%) | 13 / 43 (30.23%) | |
| occurrences causally related to treatment / all | 0 / 20 | 0 / 15 | |
| deaths causally related to treatment / all | 0 / 20 | 0 / 12 | |
| Malignant pleural effusion | | | |
| subjects affected / exposed | 2 / 93 (2.15%) | 0 / 43 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metastases to meninges | | | |
| subjects affected / exposed | 1 / 93 (1.08%) | 0 / 43 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|--|----------------|----------------|--|
| Neoplasm progression | | | |
| subjects affected / exposed | 0 / 93 (0.00%) | 1 / 43 (2.33%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Second primary malignancy | | | |
| subjects affected / exposed | 0 / 93 (0.00%) | 0 / 43 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Tumour pain | | | |
| subjects affected / exposed | 0 / 93 (0.00%) | 0 / 43 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vascular disorders | | | |
| Deep vein thrombosis | | | |
| subjects affected / exposed | 1 / 93 (1.08%) | 0 / 43 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypotension | | | |
| subjects affected / exposed | 1 / 93 (1.08%) | 0 / 43 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Orthostatic hypotension | | | |
| subjects affected / exposed | 0 / 93 (0.00%) | 0 / 43 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Superior vena cava syndrome | | | |
| subjects affected / exposed | 0 / 93 (0.00%) | 0 / 43 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General disorders and administration site conditions | | | |
| Euthanasia | | | |
| subjects affected / exposed | 0 / 93 (0.00%) | 0 / 43 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|----------------|----------------|--|
| Fatigue | | | |
| subjects affected / exposed | 0 / 93 (0.00%) | 0 / 43 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General physical health deterioration | | | |
| subjects affected / exposed | 0 / 93 (0.00%) | 0 / 43 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Influenza like illness | | | |
| subjects affected / exposed | 0 / 93 (0.00%) | 1 / 43 (2.33%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Oedema peripheral | | | |
| subjects affected / exposed | 0 / 93 (0.00%) | 0 / 43 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pain | | | |
| subjects affected / exposed | 0 / 93 (0.00%) | 0 / 43 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pyrexia | | | |
| subjects affected / exposed | 3 / 93 (3.23%) | 0 / 43 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Reproductive system and breast disorders | | | |
| Scrotal oedema | | | |
| subjects affected / exposed | 0 / 93 (0.00%) | 0 / 43 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Acute respiratory failure | | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 4 / 93 (4.30%) | 1 / 43 (2.33%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Atelectasis | | | |
| subjects affected / exposed | 1 / 93 (1.08%) | 0 / 43 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bronchial obstruction | | | |
| subjects affected / exposed | 1 / 93 (1.08%) | 0 / 43 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Chronic obstructive pulmonary disease | | | |
| subjects affected / exposed | 0 / 93 (0.00%) | 0 / 43 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dyspnoea | | | |
| subjects affected / exposed | 5 / 93 (5.38%) | 0 / 43 (0.00%) | |
| occurrences causally related to treatment / all | 2 / 5 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haemoptysis | | | |
| subjects affected / exposed | 2 / 93 (2.15%) | 0 / 43 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypoxia | | | |
| subjects affected / exposed | 1 / 93 (1.08%) | 0 / 43 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Interstitial lung disease | | | |
| subjects affected / exposed | 0 / 93 (0.00%) | 0 / 43 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lung consolidation | | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 1 / 93 (1.08%) | 0 / 43 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Oesophagobronchial fistula | | | |
| subjects affected / exposed | 1 / 93 (1.08%) | 0 / 43 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pleural effusion | | | |
| subjects affected / exposed | 3 / 93 (3.23%) | 1 / 43 (2.33%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonitis | | | |
| subjects affected / exposed | 3 / 93 (3.23%) | 3 / 43 (6.98%) | |
| occurrences causally related to treatment / all | 3 / 3 | 3 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumothorax | | | |
| subjects affected / exposed | 0 / 93 (0.00%) | 1 / 43 (2.33%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pulmonary embolism | | | |
| subjects affected / exposed | 1 / 93 (1.08%) | 1 / 43 (2.33%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Respiratory distress | | | |
| subjects affected / exposed | 1 / 93 (1.08%) | 0 / 43 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory failure | | | |
| subjects affected / exposed | 1 / 93 (1.08%) | 1 / 43 (2.33%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 1 | |
| Psychiatric disorders | | | |
| Confusional state | | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 0 / 93 (0.00%) | 1 / 43 (2.33%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Delirium | | | |
| subjects affected / exposed | 0 / 93 (0.00%) | 0 / 43 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Mental status changes | | | |
| subjects affected / exposed | 0 / 93 (0.00%) | 0 / 43 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Investigations | | | |
| Blood bilirubin increased | | | |
| subjects affected / exposed | 0 / 93 (0.00%) | 1 / 43 (2.33%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Blood creatine phosphokinase increased | | | |
| subjects affected / exposed | 0 / 93 (0.00%) | 0 / 43 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Human chorionic gonadotropin positive | | | |
| subjects affected / exposed | 1 / 93 (1.08%) | 0 / 43 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Transaminases increased | | | |
| subjects affected / exposed | 1 / 93 (1.08%) | 0 / 43 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Injury, poisoning and procedural complications | | | |
| Ankle fracture | | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 0 / 93 (0.00%) | 0 / 43 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Fall | | | |
| subjects affected / exposed | 0 / 93 (0.00%) | 0 / 43 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Humerus fracture | | | |
| subjects affected / exposed | 1 / 93 (1.08%) | 0 / 43 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infusion related reaction | | | |
| subjects affected / exposed | 0 / 93 (0.00%) | 0 / 43 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Overdose | | | |
| subjects affected / exposed | 1 / 93 (1.08%) | 2 / 43 (4.65%) | |
| occurrences causally related to treatment / all | 1 / 1 | 2 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Subdural haematoma | | | |
| subjects affected / exposed | 1 / 93 (1.08%) | 0 / 43 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Toxicity to various agents | | | |
| subjects affected / exposed | 1 / 93 (1.08%) | 0 / 43 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac disorders | | | |
| Atrial fibrillation | | | |
| subjects affected / exposed | 3 / 93 (3.23%) | 1 / 43 (2.33%) | |
| occurrences causally related to treatment / all | 1 / 7 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Atrial flutter | | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 1 / 93 (1.08%) | 0 / 43 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac arrest | | | |
| subjects affected / exposed | 0 / 93 (0.00%) | 0 / 43 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac tamponade | | | |
| subjects affected / exposed | 0 / 93 (0.00%) | 0 / 43 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Myocarditis | | | |
| subjects affected / exposed | 0 / 93 (0.00%) | 0 / 43 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pericardial effusion | | | |
| subjects affected / exposed | 1 / 93 (1.08%) | 0 / 43 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Supraventricular tachycardia | | | |
| subjects affected / exposed | 1 / 93 (1.08%) | 1 / 43 (2.33%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Tachycardia | | | |
| subjects affected / exposed | 1 / 93 (1.08%) | 0 / 43 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nervous system disorders | | | |
| Brachial plexopathy | | | |
| subjects affected / exposed | 0 / 93 (0.00%) | 0 / 43 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cerebral ischaemia | | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 1 / 93 (1.08%) | 0 / 43 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cerebrovascular accident | | | |
| subjects affected / exposed | 0 / 93 (0.00%) | 1 / 43 (2.33%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dizziness | | | |
| subjects affected / exposed | 0 / 93 (0.00%) | 0 / 43 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Facial paralysis | | | |
| subjects affected / exposed | 0 / 93 (0.00%) | 1 / 43 (2.33%) | |
| 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 / 93 (0.00%) | 0 / 43 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Headache | | | |
| subjects affected / exposed | 0 / 93 (0.00%) | 0 / 43 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ischaemic stroke | | | |
| subjects affected / exposed | 0 / 93 (0.00%) | 0 / 43 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Peripheral sensory neuropathy | | | |
| subjects affected / exposed | 0 / 93 (0.00%) | 2 / 43 (4.65%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Polyneuropathy | | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 1 / 93 (1.08%) | 0 / 43 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Seizure | | | |
| subjects affected / exposed | 1 / 93 (1.08%) | 1 / 43 (2.33%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Spinal cord compression | | | |
| subjects affected / exposed | 1 / 93 (1.08%) | 0 / 43 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Blood and lymphatic system disorders | | | |
| Neutropenia | | | |
| subjects affected / exposed | 1 / 93 (1.08%) | 1 / 43 (2.33%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Eye disorders | | | |
| Vision blurred | | | |
| subjects affected / exposed | 0 / 93 (0.00%) | 1 / 43 (2.33%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Visual impairment | | | |
| subjects affected / exposed | 0 / 93 (0.00%) | 1 / 43 (2.33%) | |
| 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 | 1 / 93 (1.08%) | 1 / 43 (2.33%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Colitis | | | |
| subjects affected / exposed | 1 / 93 (1.08%) | 0 / 43 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|----------------|----------------|--|
| Constipation | | | |
| subjects affected / exposed | 0 / 93 (0.00%) | 1 / 43 (2.33%) | |
| 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 / 93 (2.15%) | 0 / 43 (0.00%) | |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Large intestinal obstruction | | | |
| subjects affected / exposed | 0 / 93 (0.00%) | 0 / 43 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nausea | | | |
| subjects affected / exposed | 0 / 93 (0.00%) | 0 / 43 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Oesophageal food impaction | | | |
| subjects affected / exposed | 0 / 93 (0.00%) | 0 / 43 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Peritoneal haemorrhage | | | |
| subjects affected / exposed | 1 / 93 (1.08%) | 0 / 43 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vomiting | | | |
| subjects affected / exposed | 0 / 93 (0.00%) | 0 / 43 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatobiliary disorders | | | |
| Cholecystitis acute | | | |
| subjects affected / exposed | 0 / 93 (0.00%) | 0 / 43 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatitis | | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 0 / 93 (0.00%) | 0 / 43 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hyperbilirubinaemia | | | |
| subjects affected / exposed | 0 / 93 (0.00%) | 1 / 43 (2.33%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Skin and subcutaneous tissue disorders | | | |
| Stevens-Johnson syndrome | | | |
| subjects affected / exposed | 1 / 93 (1.08%) | 0 / 43 (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 / 93 (2.15%) | 0 / 43 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Endocrine disorders | | | |
| Adrenal insufficiency | | | |
| subjects affected / exposed | 0 / 93 (0.00%) | 0 / 43 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypoparathyroidism | | | |
| subjects affected / exposed | 1 / 93 (1.08%) | 0 / 43 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypophysitis | | | |
| subjects affected / exposed | 1 / 93 (1.08%) | 0 / 43 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 0 / 93 (0.00%) | 0 / 43 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Back pain | | | |
| subjects affected / exposed | 0 / 93 (0.00%) | 1 / 43 (2.33%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Flank pain | | | |
| subjects affected / exposed | 0 / 93 (0.00%) | 1 / 43 (2.33%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Muscular weakness | | | |
| subjects affected / exposed | 1 / 93 (1.08%) | 1 / 43 (2.33%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal chest pain | | | |
| subjects affected / exposed | 0 / 93 (0.00%) | 0 / 43 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Osteolysis | | | |
| subjects affected / exposed | 0 / 93 (0.00%) | 0 / 43 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pain in extremity | | | |
| subjects affected / exposed | 0 / 93 (0.00%) | 1 / 43 (2.33%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sjogren's syndrome | | | |
| subjects affected / exposed | 1 / 93 (1.08%) | 0 / 43 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Appendicitis | | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 1 / 93 (1.08%) | 0 / 43 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Brain abscess | | | |
| subjects affected / exposed | 0 / 93 (0.00%) | 0 / 43 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Clostridium difficile colitis | | | |
| subjects affected / exposed | 0 / 93 (0.00%) | 0 / 43 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Enterocolitis infectious | | | |
| subjects affected / exposed | 0 / 93 (0.00%) | 0 / 43 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Influenza | | | |
| subjects affected / exposed | 0 / 93 (0.00%) | 1 / 43 (2.33%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pharyngitis streptococcal | | | |
| subjects affected / exposed | 0 / 93 (0.00%) | 0 / 43 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia | | | |
| subjects affected / exposed | 5 / 93 (5.38%) | 1 / 43 (2.33%) | |
| occurrences causally related to treatment / all | 0 / 6 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia bacterial | | | |
| subjects affected / exposed | 1 / 93 (1.08%) | 0 / 43 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Post procedural infection | | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 0 / 93 (0.00%) | 0 / 43 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory tract infection | | | |
| subjects affected / exposed | 2 / 93 (2.15%) | 0 / 43 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sepsis | | | |
| subjects affected / exposed | 2 / 93 (2.15%) | 1 / 43 (2.33%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Septic shock | | | |
| subjects affected / exposed | 0 / 93 (0.00%) | 0 / 43 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Staphylococcal infection | | | |
| subjects affected / exposed | 0 / 93 (0.00%) | 1 / 43 (2.33%) | |
| 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 / 93 (0.00%) | 0 / 43 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metabolism and nutrition disorders | | | |
| Dehydration | | | |
| subjects affected / exposed | 0 / 93 (0.00%) | 0 / 43 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diabetes mellitus | | | |
| subjects affected / exposed | 1 / 93 (1.08%) | 0 / 43 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diabetic ketoacidosis | | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 1 / 93 (1.08%) | 0 / 43 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Failure to thrive | | | |
| subjects affected / exposed | 1 / 93 (1.08%) | 0 / 43 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypercalcaemia | | | |
| subjects affected / exposed | 1 / 93 (1.08%) | 0 / 43 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Hyperglycaemia | | | |
| subjects affected / exposed | 0 / 93 (0.00%) | 1 / 43 (2.33%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hyponatraemia | | | |
| subjects affected / exposed | 1 / 93 (1.08%) | 1 / 43 (2.33%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| Non-serious adverse events | Nivolumab | Nivolumab + Dasatinib | Nivolumab + BMS986016 |
|---|------------------|-----------------------|-----------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 46 / 49 (93.88%) | 98 / 106 (92.45%) | 18 / 18 (100.00%) |
| Vascular disorders | | | |
| Deep vein thrombosis | | | |
| subjects affected / exposed | 2 / 49 (4.08%) | 1 / 106 (0.94%) | 1 / 18 (5.56%) |
| occurrences (all) | 2 | 1 | 1 |
| Hypertension | | | |
| subjects affected / exposed | 2 / 49 (4.08%) | 6 / 106 (5.66%) | 0 / 18 (0.00%) |
| occurrences (all) | 2 | 9 | 0 |
| Hypotension | | | |

| | | | |
|---|---------------------|----------------------|---------------------|
| subjects affected / exposed occurrences (all) | 3 / 49 (6.12%) 3 | 2 / 106 (1.89%) 2 | 0 / 18 (0.00%) 0 |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 7 / 49 (14.29%) | 18 / 106 (16.98%) | 0 / 18 (0.00%) |
| occurrences (all) | 9 | 21 | 0 |
| Chest discomfort | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 2 / 106 (1.89%) | 2 / 18 (11.11%) |
| occurrences (all) | 0 | 2 | 2 |
| Chest pain | | | |
| subjects affected / exposed | 4 / 49 (8.16%) | 7 / 106 (6.60%) | 1 / 18 (5.56%) |
| occurrences (all) | 5 | 7 | 1 |
| Chills | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 11 / 106 (10.38%) | 1 / 18 (5.56%) |
| occurrences (all) | 0 | 15 | 1 |
| Early satiety | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 2 / 106 (1.89%) | 1 / 18 (5.56%) |
| occurrences (all) | 0 | 2 | 1 |
| Fatigue | | | |
| subjects affected / exposed | 17 / 49 (34.69%) | 51 / 106 (48.11%) | 5 / 18 (27.78%) |
| occurrences (all) | 24 | 53 | 5 |
| Oedema | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 7 / 106 (6.60%) | 0 / 18 (0.00%) |
| occurrences (all) | 0 | 8 | 0 |
| Oedema peripheral | | | |
| subjects affected / exposed | 7 / 49 (14.29%) | 8 / 106 (7.55%) | 1 / 18 (5.56%) |
| occurrences (all) | 9 | 9 | 1 |
| Pyrexia | | | |
| subjects affected / exposed | 4 / 49 (8.16%) | 18 / 106 (16.98%) | 1 / 18 (5.56%) |
| occurrences (all) | 6 | 30 | 1 |
| Non-Cardiac chest pain | | | |
| subjects affected / exposed | 1 / 49 (2.04%) | 6 / 106 (5.66%) | 0 / 18 (0.00%) |
| occurrences (all) | 1 | 6 | 0 |
| Immune system disorders | | | |

| | | | |
|--|------------------------|-------------------------|----------------------|
| Hypersensitivity subjects affected / exposed occurrences (all) | 0 / 49 (0.00%) 0 | 1 / 106 (0.94%) 1 | 1 / 18 (5.56%) 1 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough subjects affected / exposed occurrences (all) | 12 / 49 (24.49%) 14 | 21 / 106 (19.81%) 24 | 2 / 18 (11.11%) 2 |
| Dyspnoea subjects affected / exposed occurrences (all) | 16 / 49 (32.65%) 18 | 34 / 106 (32.08%) 40 | 1 / 18 (5.56%) 1 |
| Dyspnoea exertional subjects affected / exposed occurrences (all) | 2 / 49 (4.08%) 2 | 8 / 106 (7.55%) 8 | 2 / 18 (11.11%) 2 |
| Haemoptysis subjects affected / exposed occurrences (all) | 6 / 49 (12.24%) 7 | 8 / 106 (7.55%) 8 | 0 / 18 (0.00%) 0 |
| Hypoxia subjects affected / exposed occurrences (all) | 2 / 49 (4.08%) 2 | 6 / 106 (5.66%) 6 | 0 / 18 (0.00%) 0 |
| Nasal congestion subjects affected / exposed occurrences (all) | 1 / 49 (2.04%) 1 | 2 / 106 (1.89%) 2 | 0 / 18 (0.00%) 0 |
| Oropharyngeal pain subjects affected / exposed occurrences (all) | 2 / 49 (4.08%) 2 | 1 / 106 (0.94%) 1 | 0 / 18 (0.00%) 0 |
| Pleural effusion subjects affected / exposed occurrences (all) | 2 / 49 (4.08%) 2 | 20 / 106 (18.87%) 26 | 1 / 18 (5.56%) 1 |
| Pneumonia aspiration subjects affected / exposed occurrences (all) | 0 / 49 (0.00%) 0 | 0 / 106 (0.00%) 0 | 1 / 18 (5.56%) 1 |
| Pneumonitis subjects affected / exposed occurrences (all) | 1 / 49 (2.04%) 1 | 3 / 106 (2.83%) 4 | 1 / 18 (5.56%) 1 |
| Productive cough | | | |

| | | | |
|--|----------------------|-------------------------|---------------------|
| subjects affected / exposed occurrences (all) | 7 / 49 (14.29%) 9 | 11 / 106 (10.38%) 13 | 0 / 18 (0.00%) 0 |
| Pulmonary embolism subjects affected / exposed occurrences (all) | 0 / 49 (0.00%) 0 | 2 / 106 (1.89%) 2 | 1 / 18 (5.56%) 1 |
| Wheezing subjects affected / exposed occurrences (all) | 0 / 49 (0.00%) 0 | 0 / 106 (0.00%) 0 | 0 / 18 (0.00%) 0 |
| Upper-Airway cough syndrome subjects affected / exposed occurrences (all) | 0 / 49 (0.00%) 0 | 1 / 106 (0.94%) 1 | 1 / 18 (5.56%) 1 |
| Psychiatric disorders | | | |
| Anxiety subjects affected / exposed occurrences (all) | 7 / 49 (14.29%) 7 | 15 / 106 (14.15%) 15 | 0 / 18 (0.00%) 0 |
| Confusional state subjects affected / exposed occurrences (all) | 3 / 49 (6.12%) 4 | 5 / 106 (4.72%) 5 | 0 / 18 (0.00%) 0 |
| Depression subjects affected / exposed occurrences (all) | 2 / 49 (4.08%) 2 | 5 / 106 (4.72%) 5 | 0 / 18 (0.00%) 0 |
| Insomnia subjects affected / exposed occurrences (all) | 7 / 49 (14.29%) 8 | 11 / 106 (10.38%) 11 | 0 / 18 (0.00%) 0 |
| Investigations | | | |
| Alanine aminotransferase increased subjects affected / exposed occurrences (all) | 4 / 49 (8.16%) 5 | 8 / 106 (7.55%) 8 | 0 / 18 (0.00%) 0 |
| Amylase increased subjects affected / exposed occurrences (all) | 4 / 49 (8.16%) 7 | 8 / 106 (7.55%) 9 | 1 / 18 (5.56%) 1 |
| Aspartate aminotransferase increased subjects affected / exposed occurrences (all) | 6 / 49 (12.24%) 7 | 7 / 106 (6.60%) 7 | 1 / 18 (5.56%) 1 |
| Blood alkaline phosphatase increased | | | |

| | | | |
|--|-----------------|-------------------|----------------|
| subjects affected / exposed | 3 / 49 (6.12%) | 3 / 106 (2.83%) | 0 / 18 (0.00%) |
| occurrences (all) | 3 | 3 | 0 |
| Blood bilirubin increased | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 0 / 106 (0.00%) | 0 / 18 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood creatinine increased | | | |
| subjects affected / exposed | 2 / 49 (4.08%) | 3 / 106 (2.83%) | 1 / 18 (5.56%) |
| occurrences (all) | 2 | 3 | 1 |
| Blood thyroid stimulating hormone increased | | | |
| subjects affected / exposed | 2 / 49 (4.08%) | 0 / 106 (0.00%) | 1 / 18 (5.56%) |
| occurrences (all) | 2 | 0 | 1 |
| Lipase increased | | | |
| subjects affected / exposed | 2 / 49 (4.08%) | 6 / 106 (5.66%) | 0 / 18 (0.00%) |
| occurrences (all) | 2 | 6 | 0 |
| Lymphocyte count decreased | | | |
| subjects affected / exposed | 2 / 49 (4.08%) | 2 / 106 (1.89%) | 1 / 18 (5.56%) |
| occurrences (all) | 3 | 3 | 1 |
| Weight decreased | | | |
| subjects affected / exposed | 7 / 49 (14.29%) | 18 / 106 (16.98%) | 0 / 18 (0.00%) |
| occurrences (all) | 7 | 19 | 0 |
| Injury, poisoning and procedural complications | | | |
| Contusion | | | |
| subjects affected / exposed | 1 / 49 (2.04%) | 3 / 106 (2.83%) | 1 / 18 (5.56%) |
| occurrences (all) | 1 | 3 | 1 |
| Cardiac disorders | | | |
| Tachycardia | | | |
| subjects affected / exposed | 3 / 49 (6.12%) | 4 / 106 (3.77%) | 0 / 18 (0.00%) |
| occurrences (all) | 4 | 5 | 0 |
| Nervous system disorders | | | |
| Dizziness | | | |
| subjects affected / exposed | 7 / 49 (14.29%) | 14 / 106 (13.21%) | 1 / 18 (5.56%) |
| occurrences (all) | 7 | 14 | 1 |
| Dizziness postural | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 0 / 106 (0.00%) | 1 / 18 (5.56%) |
| occurrences (all) | 0 | 0 | 1 |
| Dysgeusia | | | |

| | | | |
|--------------------------------------|------------------|-------------------|-----------------|
| subjects affected / exposed | 2 / 49 (4.08%) | 10 / 106 (9.43%) | 0 / 18 (0.00%) |
| occurrences (all) | 2 | 11 | 0 |
| Headache | | | |
| subjects affected / exposed | 12 / 49 (24.49%) | 16 / 106 (15.09%) | 2 / 18 (11.11%) |
| occurrences (all) | 14 | 18 | 2 |
| Hypoaesthesia | | | |
| subjects affected / exposed | 3 / 49 (6.12%) | 2 / 106 (1.89%) | 0 / 18 (0.00%) |
| occurrences (all) | 3 | 3 | 0 |
| Peripheral motor neuropathy | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 2 / 106 (1.89%) | 1 / 18 (5.56%) |
| occurrences (all) | 0 | 3 | 1 |
| Peripheral sensory neuropathy | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 4 / 106 (3.77%) | 1 / 18 (5.56%) |
| occurrences (all) | 0 | 4 | 1 |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 8 / 49 (16.33%) | 25 / 106 (23.58%) | 2 / 18 (11.11%) |
| occurrences (all) | 11 | 34 | 2 |
| Eye disorders | | | |
| Vision blurred | | | |
| subjects affected / exposed | 3 / 49 (6.12%) | 3 / 106 (2.83%) | 0 / 18 (0.00%) |
| occurrences (all) | 3 | 4 | 0 |
| Gastrointestinal disorders | | | |
| Abdominal discomfort | | | |
| subjects affected / exposed | 1 / 49 (2.04%) | 1 / 106 (0.94%) | 1 / 18 (5.56%) |
| occurrences (all) | 1 | 1 | 1 |
| Abdominal distension | | | |
| subjects affected / exposed | 1 / 49 (2.04%) | 1 / 106 (0.94%) | 0 / 18 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Abdominal pain | | | |
| subjects affected / exposed | 5 / 49 (10.20%) | 11 / 106 (10.38%) | 2 / 18 (11.11%) |
| occurrences (all) | 7 | 15 | 2 |
| Abdominal pain upper | | | |
| subjects affected / exposed | 3 / 49 (6.12%) | 1 / 106 (0.94%) | 0 / 18 (0.00%) |
| occurrences (all) | 3 | 1 | 0 |
| Constipation | | | |

| | | | |
|--|------------------|-------------------|-----------------|
| subjects affected / exposed | 9 / 49 (18.37%) | 33 / 106 (31.13%) | 1 / 18 (5.56%) |
| occurrences (all) | 11 | 38 | 1 |
| Diarrhoea | | | |
| subjects affected / exposed | 15 / 49 (30.61%) | 32 / 106 (30.19%) | 5 / 18 (27.78%) |
| occurrences (all) | 25 | 43 | 5 |
| Dry mouth | | | |
| subjects affected / exposed | 1 / 49 (2.04%) | 1 / 106 (0.94%) | 2 / 18 (11.11%) |
| occurrences (all) | 1 | 1 | 2 |
| Dyspepsia | | | |
| subjects affected / exposed | 3 / 49 (6.12%) | 3 / 106 (2.83%) | 1 / 18 (5.56%) |
| occurrences (all) | 3 | 4 | 1 |
| Mouth ulceration | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 0 / 106 (0.00%) | 1 / 18 (5.56%) |
| occurrences (all) | 0 | 0 | 1 |
| Nausea | | | |
| subjects affected / exposed | 17 / 49 (34.69%) | 45 / 106 (42.45%) | 3 / 18 (16.67%) |
| occurrences (all) | 20 | 60 | 3 |
| Stomatitis | | | |
| subjects affected / exposed | 1 / 49 (2.04%) | 4 / 106 (3.77%) | 2 / 18 (11.11%) |
| occurrences (all) | 3 | 4 | 2 |
| Tongue dysplasia | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 0 / 106 (0.00%) | 1 / 18 (5.56%) |
| occurrences (all) | 0 | 0 | 1 |
| Vomiting | | | |
| subjects affected / exposed | 9 / 49 (18.37%) | 26 / 106 (24.53%) | 1 / 18 (5.56%) |
| occurrences (all) | 11 | 30 | 2 |
| Hepatobiliary disorders | | | |
| Cholelithiasis | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 0 / 106 (0.00%) | 1 / 18 (5.56%) |
| occurrences (all) | 0 | 0 | 1 |
| Skin and subcutaneous tissue disorders | | | |
| Alopecia | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 6 / 106 (5.66%) | 1 / 18 (5.56%) |
| occurrences (all) | 0 | 6 | 1 |
| Dry skin | | | |

| | | | |
|---|------------------|-------------------|-----------------|
| subjects affected / exposed | 4 / 49 (8.16%) | 6 / 106 (5.66%) | 1 / 18 (5.56%) |
| occurrences (all) | 4 | 6 | 1 |
| Hyperhidrosis | | | |
| subjects affected / exposed | 2 / 49 (4.08%) | 2 / 106 (1.89%) | 0 / 18 (0.00%) |
| occurrences (all) | 2 | 3 | 0 |
| Night sweats | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 1 / 106 (0.94%) | 1 / 18 (5.56%) |
| occurrences (all) | 0 | 1 | 1 |
| Pruritus | | | |
| subjects affected / exposed | 8 / 49 (16.33%) | 11 / 106 (10.38%) | 1 / 18 (5.56%) |
| occurrences (all) | 12 | 15 | 1 |
| Rash | | | |
| subjects affected / exposed | 5 / 49 (10.20%) | 17 / 106 (16.04%) | 3 / 18 (16.67%) |
| occurrences (all) | 7 | 19 | 3 |
| Rash maculo-papular | | | |
| subjects affected / exposed | 2 / 49 (4.08%) | 2 / 106 (1.89%) | 0 / 18 (0.00%) |
| occurrences (all) | 2 | 2 | 0 |
| Rash pruritic | | | |
| subjects affected / exposed | 1 / 49 (2.04%) | 4 / 106 (3.77%) | 1 / 18 (5.56%) |
| occurrences (all) | 1 | 4 | 1 |
| Endocrine disorders | | | |
| Hyperthyroidism | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 2 / 106 (1.89%) | 1 / 18 (5.56%) |
| occurrences (all) | 0 | 2 | 1 |
| Hypothyroidism | | | |
| subjects affected / exposed | 4 / 49 (8.16%) | 4 / 106 (3.77%) | 0 / 18 (0.00%) |
| occurrences (all) | 4 | 4 | 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 12 / 49 (24.49%) | 11 / 106 (10.38%) | 1 / 18 (5.56%) |
| occurrences (all) | 14 | 14 | 1 |
| Back pain | | | |
| subjects affected / exposed | 10 / 49 (20.41%) | 17 / 106 (16.04%) | 1 / 18 (5.56%) |
| occurrences (all) | 11 | 18 | 1 |
| Flank pain | | | |

| | | | |
|-----------------------------|-----------------|-------------------|----------------|
| subjects affected / exposed | 0 / 49 (0.00%) | 5 / 106 (4.72%) | 1 / 18 (5.56%) |
| occurrences (all) | 0 | 5 | 1 |
| Musculoskeletal chest pain | | | |
| subjects affected / exposed | 3 / 49 (6.12%) | 7 / 106 (6.60%) | 1 / 18 (5.56%) |
| occurrences (all) | 3 | 7 | 1 |
| Musculoskeletal pain | | | |
| subjects affected / exposed | 8 / 49 (16.33%) | 10 / 106 (9.43%) | 1 / 18 (5.56%) |
| occurrences (all) | 8 | 11 | 1 |
| Musculoskeletal stiffness | | | |
| subjects affected / exposed | 3 / 49 (6.12%) | 0 / 106 (0.00%) | 0 / 18 (0.00%) |
| occurrences (all) | 3 | 0 | 0 |
| Myalgia | | | |
| subjects affected / exposed | 4 / 49 (8.16%) | 6 / 106 (5.66%) | 1 / 18 (5.56%) |
| occurrences (all) | 5 | 6 | 1 |
| Neck pain | | | |
| subjects affected / exposed | 1 / 49 (2.04%) | 6 / 106 (5.66%) | 1 / 18 (5.56%) |
| occurrences (all) | 1 | 6 | 1 |
| Pain in extremity | | | |
| subjects affected / exposed | 7 / 49 (14.29%) | 11 / 106 (10.38%) | 0 / 18 (0.00%) |
| occurrences (all) | 8 | 13 | 0 |
| Spinal pain | | | |
| subjects affected / exposed | 3 / 49 (6.12%) | 0 / 106 (0.00%) | 0 / 18 (0.00%) |
| occurrences (all) | 3 | 0 | 0 |
| Infections and infestations | | | |
| Bronchitis | | | |
| subjects affected / exposed | 1 / 49 (2.04%) | 1 / 106 (0.94%) | 1 / 18 (5.56%) |
| occurrences (all) | 2 | 2 | 1 |
| Influenza | | | |
| subjects affected / exposed | 2 / 49 (4.08%) | 0 / 106 (0.00%) | 0 / 18 (0.00%) |
| occurrences (all) | 3 | 0 | 0 |
| Laryngitis | | | |
| subjects affected / exposed | 0 / 49 (0.00%) | 0 / 106 (0.00%) | 1 / 18 (5.56%) |
| occurrences (all) | 0 | 0 | 1 |
| Nasopharyngitis | | | |
| subjects affected / exposed | 2 / 49 (4.08%) | 6 / 106 (5.66%) | 0 / 18 (0.00%) |
| occurrences (all) | 2 | 7 | 0 |

| | | | |
|------------------------------------|------------------|-------------------|-----------------|
| Pneumonia | | | |
| subjects affected / exposed | 3 / 49 (6.12%) | 6 / 106 (5.66%) | 0 / 18 (0.00%) |
| occurrences (all) | 4 | 6 | 0 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 3 / 49 (6.12%) | 4 / 106 (3.77%) | 1 / 18 (5.56%) |
| occurrences (all) | 4 | 5 | 1 |
| Urinary tract infection | | | |
| subjects affected / exposed | 7 / 49 (14.29%) | 2 / 106 (1.89%) | 0 / 18 (0.00%) |
| occurrences (all) | 8 | 2 | 0 |
| Metabolism and nutrition disorders | | | |
| Decreased appetite | | | |
| subjects affected / exposed | 18 / 49 (36.73%) | 39 / 106 (36.79%) | 5 / 18 (27.78%) |
| occurrences (all) | 22 | 44 | 5 |
| Dehydration | | | |
| subjects affected / exposed | 1 / 49 (2.04%) | 6 / 106 (5.66%) | 0 / 18 (0.00%) |
| occurrences (all) | 1 | 6 | 0 |
| Hyperglycaemia | | | |
| subjects affected / exposed | 1 / 49 (2.04%) | 3 / 106 (2.83%) | 1 / 18 (5.56%) |
| occurrences (all) | 4 | 3 | 1 |
| Hyperkalaemia | | | |
| subjects affected / exposed | 1 / 49 (2.04%) | 1 / 106 (0.94%) | 0 / 18 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Hypocalcaemia | | | |
| subjects affected / exposed | 3 / 49 (6.12%) | 2 / 106 (1.89%) | 0 / 18 (0.00%) |
| occurrences (all) | 5 | 2 | 0 |
| Hypokalaemia | | | |
| subjects affected / exposed | 4 / 49 (8.16%) | 6 / 106 (5.66%) | 1 / 18 (5.56%) |
| occurrences (all) | 5 | 8 | 1 |
| Hypomagnesaemia | | | |
| subjects affected / exposed | 5 / 49 (10.20%) | 8 / 106 (7.55%) | 0 / 18 (0.00%) |
| occurrences (all) | 5 | 9 | 0 |
| Hyponatraemia | | | |
| subjects affected / exposed | 6 / 49 (12.24%) | 10 / 106 (9.43%) | 1 / 18 (5.56%) |
| occurrences (all) | 6 | 13 | 1 |
| Hypophosphataemia | | | |

| | | | |
|-----------------------------|----------------|-----------------|----------------|
| subjects affected / exposed | 3 / 49 (6.12%) | 9 / 106 (8.49%) | 0 / 18 (0.00%) |
| occurrences (all) | 3 | 14 | 0 |

| Non-serious adverse events | Nivolumab + Ipilimumab | Nivolumab + BMS986205 | |
|---|---------------------------|--------------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 91 / 93 (97.85%) | 41 / 43 (95.35%) | |
| Vascular disorders | | | |
| Deep vein thrombosis | | | |
| subjects affected / exposed | 0 / 93 (0.00%) | 0 / 43 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Hypertension | | | |
| subjects affected / exposed | 5 / 93 (5.38%) | 6 / 43 (13.95%) | |
| occurrences (all) | 7 | 7 | |
| Hypotension | | | |
| subjects affected / exposed | 6 / 93 (6.45%) | 2 / 43 (4.65%) | |
| occurrences (all) | 8 | 2 | |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 11 / 93 (11.83%) | 1 / 43 (2.33%) | |
| occurrences (all) | 16 | 1 | |
| Chest discomfort | | | |
| subjects affected / exposed | 3 / 93 (3.23%) | 1 / 43 (2.33%) | |
| occurrences (all) | 3 | 1 | |
| Chest pain | | | |
| subjects affected / exposed | 5 / 93 (5.38%) | 2 / 43 (4.65%) | |
| occurrences (all) | 6 | 3 | |
| Chills | | | |
| subjects affected / exposed | 5 / 93 (5.38%) | 1 / 43 (2.33%) | |
| occurrences (all) | 5 | 3 | |
| Early satiety | | | |
| subjects affected / exposed | 1 / 93 (1.08%) | 0 / 43 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Fatigue | | | |
| subjects affected / exposed | 44 / 93 (47.31%) | 20 / 43 (46.51%) | |
| occurrences (all) | 52 | 25 | |
| Oedema | | | |

| | | | |
|--|------------------------|------------------------|--|
| subjects affected / exposed occurrences (all) | 1 / 93 (1.08%) 1 | 2 / 43 (4.65%) 2 | |
| Oedema peripheral subjects affected / exposed occurrences (all) | 8 / 93 (8.60%) 10 | 7 / 43 (16.28%) 9 | |
| Pyrexia subjects affected / exposed occurrences (all) | 15 / 93 (16.13%) 23 | 5 / 43 (11.63%) 7 | |
| Non-Cardiac chest pain subjects affected / exposed occurrences (all) | 5 / 93 (5.38%) 6 | 0 / 43 (0.00%) 0 | |
| Immune system disorders Hypersensitivity subjects affected / exposed occurrences (all) | 0 / 93 (0.00%) 0 | 0 / 43 (0.00%) 0 | |
| Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) | 25 / 93 (26.88%) 28 | 11 / 43 (25.58%) 11 | |
| Dyspnoea subjects affected / exposed occurrences (all) | 27 / 93 (29.03%) 32 | 6 / 43 (13.95%) 9 | |
| Dyspnoea exertional subjects affected / exposed occurrences (all) | 4 / 93 (4.30%) 4 | 1 / 43 (2.33%) 1 | |
| Haemoptysis subjects affected / exposed occurrences (all) | 4 / 93 (4.30%) 6 | 2 / 43 (4.65%) 2 | |
| Hypoxia subjects affected / exposed occurrences (all) | 6 / 93 (6.45%) 6 | 1 / 43 (2.33%) 2 | |
| Nasal congestion subjects affected / exposed occurrences (all) | 5 / 93 (5.38%) 5 | 1 / 43 (2.33%) 1 | |
| Oropharyngeal pain | | | |

| | | | |
|-----------------------------|------------------|-----------------|--|
| subjects affected / exposed | 5 / 93 (5.38%) | 0 / 43 (0.00%) | |
| occurrences (all) | 6 | 0 | |
| Pleural effusion | | | |
| subjects affected / exposed | 4 / 93 (4.30%) | 3 / 43 (6.98%) | |
| occurrences (all) | 4 | 3 | |
| Pneumonia aspiration | | | |
| subjects affected / exposed | 0 / 93 (0.00%) | 0 / 43 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Pneumonitis | | | |
| subjects affected / exposed | 4 / 93 (4.30%) | 2 / 43 (4.65%) | |
| occurrences (all) | 4 | 3 | |
| Productive cough | | | |
| subjects affected / exposed | 7 / 93 (7.53%) | 2 / 43 (4.65%) | |
| occurrences (all) | 8 | 2 | |
| Pulmonary embolism | | | |
| subjects affected / exposed | 3 / 93 (3.23%) | 0 / 43 (0.00%) | |
| occurrences (all) | 3 | 0 | |
| Wheezing | | | |
| subjects affected / exposed | 6 / 93 (6.45%) | 2 / 43 (4.65%) | |
| occurrences (all) | 6 | 2 | |
| Upper-Airway cough syndrome | | | |
| subjects affected / exposed | 3 / 93 (3.23%) | 1 / 43 (2.33%) | |
| occurrences (all) | 3 | 1 | |
| Psychiatric disorders | | | |
| Anxiety | | | |
| subjects affected / exposed | 8 / 93 (8.60%) | 2 / 43 (4.65%) | |
| occurrences (all) | 9 | 2 | |
| Confusional state | | | |
| subjects affected / exposed | 3 / 93 (3.23%) | 2 / 43 (4.65%) | |
| occurrences (all) | 3 | 2 | |
| Depression | | | |
| subjects affected / exposed | 5 / 93 (5.38%) | 0 / 43 (0.00%) | |
| occurrences (all) | 5 | 0 | |
| Insomnia | | | |
| subjects affected / exposed | 12 / 93 (12.90%) | 5 / 43 (11.63%) | |
| occurrences (all) | 12 | 6 | |

| | | | |
|--|------------------|------------------|--|
| Investigations | | | |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 5 / 93 (5.38%) | 5 / 43 (11.63%) | |
| occurrences (all) | 5 | 6 | |
| Amylase increased | | | |
| subjects affected / exposed | 8 / 93 (8.60%) | 0 / 43 (0.00%) | |
| occurrences (all) | 9 | 0 | |
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 6 / 93 (6.45%) | 4 / 43 (9.30%) | |
| occurrences (all) | 6 | 4 | |
| Blood alkaline phosphatase increased | | | |
| subjects affected / exposed | 4 / 93 (4.30%) | 1 / 43 (2.33%) | |
| occurrences (all) | 6 | 1 | |
| Blood bilirubin increased | | | |
| subjects affected / exposed | 1 / 93 (1.08%) | 4 / 43 (9.30%) | |
| occurrences (all) | 1 | 4 | |
| Blood creatinine increased | | | |
| subjects affected / exposed | 5 / 93 (5.38%) | 2 / 43 (4.65%) | |
| occurrences (all) | 6 | 3 | |
| Blood thyroid stimulating hormone increased | | | |
| subjects affected / exposed | 2 / 93 (2.15%) | 0 / 43 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Lipase increased | | | |
| subjects affected / exposed | 8 / 93 (8.60%) | 2 / 43 (4.65%) | |
| occurrences (all) | 9 | 2 | |
| Lymphocyte count decreased | | | |
| subjects affected / exposed | 3 / 93 (3.23%) | 3 / 43 (6.98%) | |
| occurrences (all) | 5 | 3 | |
| Weight decreased | | | |
| subjects affected / exposed | 15 / 93 (16.13%) | 13 / 43 (30.23%) | |
| occurrences (all) | 17 | 14 | |
| Injury, poisoning and procedural complications | | | |
| Contusion | | | |
| subjects affected / exposed | 0 / 93 (0.00%) | 2 / 43 (4.65%) | |
| occurrences (all) | 0 | 2 | |

| | | | |
|--------------------------------------|------------------|-----------------|--|
| Cardiac disorders | | | |
| Tachycardia | | | |
| subjects affected / exposed | 5 / 93 (5.38%) | 1 / 43 (2.33%) | |
| occurrences (all) | 6 | 1 | |
| Nervous system disorders | | | |
| Dizziness | | | |
| subjects affected / exposed | 15 / 93 (16.13%) | 3 / 43 (6.98%) | |
| occurrences (all) | 18 | 3 | |
| Dizziness postural | | | |
| subjects affected / exposed | 0 / 93 (0.00%) | 0 / 43 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Dysgeusia | | | |
| subjects affected / exposed | 2 / 93 (2.15%) | 2 / 43 (4.65%) | |
| occurrences (all) | 2 | 2 | |
| Headache | | | |
| subjects affected / exposed | 14 / 93 (15.05%) | 8 / 43 (18.60%) | |
| occurrences (all) | 21 | 10 | |
| Hypoaesthesia | | | |
| subjects affected / exposed | 1 / 93 (1.08%) | 1 / 43 (2.33%) | |
| occurrences (all) | 1 | 1 | |
| Peripheral motor neuropathy | | | |
| subjects affected / exposed | 0 / 93 (0.00%) | 0 / 43 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Peripheral sensory neuropathy | | | |
| subjects affected / exposed | 4 / 93 (4.30%) | 2 / 43 (4.65%) | |
| occurrences (all) | 4 | 2 | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 14 / 93 (15.05%) | 6 / 43 (13.95%) | |
| occurrences (all) | 16 | 7 | |
| Eye disorders | | | |
| Vision blurred | | | |
| subjects affected / exposed | 5 / 93 (5.38%) | 1 / 43 (2.33%) | |
| occurrences (all) | 5 | 1 | |
| Gastrointestinal disorders | | | |
| Abdominal discomfort | | | |

| | | |
|-----------------------------|------------------|------------------|
| subjects affected / exposed | 0 / 93 (0.00%) | 2 / 43 (4.65%) |
| occurrences (all) | 0 | 2 |
| Abdominal distension | | |
| subjects affected / exposed | 5 / 93 (5.38%) | 2 / 43 (4.65%) |
| occurrences (all) | 5 | 2 |
| Abdominal pain | | |
| subjects affected / exposed | 12 / 93 (12.90%) | 6 / 43 (13.95%) |
| occurrences (all) | 14 | 6 |
| Abdominal pain upper | | |
| subjects affected / exposed | 4 / 93 (4.30%) | 2 / 43 (4.65%) |
| occurrences (all) | 4 | 2 |
| Constipation | | |
| subjects affected / exposed | 26 / 93 (27.96%) | 13 / 43 (30.23%) |
| occurrences (all) | 29 | 14 |
| Diarrhoea | | |
| subjects affected / exposed | 24 / 93 (25.81%) | 11 / 43 (25.58%) |
| occurrences (all) | 36 | 13 |
| Dry mouth | | |
| subjects affected / exposed | 5 / 93 (5.38%) | 0 / 43 (0.00%) |
| occurrences (all) | 6 | 0 |
| Dyspepsia | | |
| subjects affected / exposed | 4 / 93 (4.30%) | 1 / 43 (2.33%) |
| occurrences (all) | 4 | 1 |
| Mouth ulceration | | |
| subjects affected / exposed | 0 / 93 (0.00%) | 0 / 43 (0.00%) |
| occurrences (all) | 0 | 0 |
| Nausea | | |
| subjects affected / exposed | 27 / 93 (29.03%) | 16 / 43 (37.21%) |
| occurrences (all) | 33 | 18 |
| Stomatitis | | |
| subjects affected / exposed | 0 / 93 (0.00%) | 3 / 43 (6.98%) |
| occurrences (all) | 0 | 3 |
| Tongue dysplasia | | |
| subjects affected / exposed | 0 / 93 (0.00%) | 0 / 43 (0.00%) |
| occurrences (all) | 0 | 0 |
| Vomiting | | |

| | | | |
|--|------------------------|----------------------|--|
| subjects affected / exposed occurrences (all) | 20 / 93 (21.51%) 30 | 5 / 43 (11.63%) 6 | |
| Hepatobiliary disorders | | | |
| Cholelithiasis | | | |
| subjects affected / exposed occurrences (all) | 0 / 93 (0.00%) 0 | 0 / 43 (0.00%) 0 | |
| Skin and subcutaneous tissue disorders | | | |
| Alopecia | | | |
| subjects affected / exposed occurrences (all) | 3 / 93 (3.23%) 3 | 3 / 43 (6.98%) 3 | |
| Dry skin | | | |
| subjects affected / exposed occurrences (all) | 8 / 93 (8.60%) 11 | 3 / 43 (6.98%) 3 | |
| Hyperhidrosis | | | |
| subjects affected / exposed occurrences (all) | 1 / 93 (1.08%) 1 | 3 / 43 (6.98%) 4 | |
| Night sweats | | | |
| subjects affected / exposed occurrences (all) | 3 / 93 (3.23%) 3 | 0 / 43 (0.00%) 0 | |
| Pruritus | | | |
| subjects affected / exposed occurrences (all) | 22 / 93 (23.66%) 28 | 3 / 43 (6.98%) 3 | |
| Rash | | | |
| subjects affected / exposed occurrences (all) | 15 / 93 (16.13%) 19 | 3 / 43 (6.98%) 3 | |
| Rash maculo-papular | | | |
| subjects affected / exposed occurrences (all) | 9 / 93 (9.68%) 11 | 2 / 43 (4.65%) 2 | |
| Rash pruritic | | | |
| subjects affected / exposed occurrences (all) | 2 / 93 (2.15%) 3 | 0 / 43 (0.00%) 0 | |
| Endocrine disorders | | | |
| Hyperthyroidism | | | |
| subjects affected / exposed occurrences (all) | 3 / 93 (3.23%) 4 | 0 / 43 (0.00%) 0 | |
| Hypothyroidism | | | |

| | | | |
|--|---------------------|---------------------|--|
| subjects affected / exposed occurrences (all) | 9 / 93 (9.68%) 9 | 1 / 43 (2.33%) 1 | |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 15 / 93 (16.13%) | 6 / 43 (13.95%) | |
| occurrences (all) | 15 | 7 | |
| Back pain | | | |
| subjects affected / exposed | 19 / 93 (20.43%) | 8 / 43 (18.60%) | |
| occurrences (all) | 20 | 8 | |
| Flank pain | | | |
| subjects affected / exposed | 3 / 93 (3.23%) | 2 / 43 (4.65%) | |
| occurrences (all) | 3 | 2 | |
| Musculoskeletal chest pain | | | |
| subjects affected / exposed | 4 / 93 (4.30%) | 1 / 43 (2.33%) | |
| occurrences (all) | 4 | 1 | |
| Musculoskeletal pain | | | |
| subjects affected / exposed | 8 / 93 (8.60%) | 5 / 43 (11.63%) | |
| occurrences (all) | 8 | 5 | |
| Musculoskeletal stiffness | | | |
| subjects affected / exposed | 0 / 93 (0.00%) | 0 / 43 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Myalgia | | | |
| subjects affected / exposed | 5 / 93 (5.38%) | 5 / 43 (11.63%) | |
| occurrences (all) | 5 | 5 | |
| Neck pain | | | |
| subjects affected / exposed | 1 / 93 (1.08%) | 0 / 43 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Pain in extremity | | | |
| subjects affected / exposed | 4 / 93 (4.30%) | 3 / 43 (6.98%) | |
| occurrences (all) | 5 | 3 | |
| Spinal pain | | | |
| subjects affected / exposed | 0 / 93 (0.00%) | 0 / 43 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Infections and infestations | | | |

| | | | |
|------------------------------------|------------------|------------------|--|
| Bronchitis | | | |
| subjects affected / exposed | 3 / 93 (3.23%) | 0 / 43 (0.00%) | |
| occurrences (all) | 4 | 0 | |
| Influenza | | | |
| subjects affected / exposed | 1 / 93 (1.08%) | 3 / 43 (6.98%) | |
| occurrences (all) | 2 | 3 | |
| Laryngitis | | | |
| subjects affected / exposed | 0 / 93 (0.00%) | 0 / 43 (0.00%) | |
| occurrences (all) | 0 | 0 | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 2 / 93 (2.15%) | 1 / 43 (2.33%) | |
| occurrences (all) | 2 | 1 | |
| Pneumonia | | | |
| subjects affected / exposed | 3 / 93 (3.23%) | 2 / 43 (4.65%) | |
| occurrences (all) | 3 | 3 | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 1 / 93 (1.08%) | 4 / 43 (9.30%) | |
| occurrences (all) | 2 | 4 | |
| Urinary tract infection | | | |
| subjects affected / exposed | 3 / 93 (3.23%) | 1 / 43 (2.33%) | |
| occurrences (all) | 6 | 1 | |
| Metabolism and nutrition disorders | | | |
| Decreased appetite | | | |
| subjects affected / exposed | 24 / 93 (25.81%) | 15 / 43 (34.88%) | |
| occurrences (all) | 30 | 17 | |
| Dehydration | | | |
| subjects affected / exposed | 5 / 93 (5.38%) | 4 / 43 (9.30%) | |
| occurrences (all) | 5 | 4 | |
| Hyperglycaemia | | | |
| subjects affected / exposed | 4 / 93 (4.30%) | 3 / 43 (6.98%) | |
| occurrences (all) | 5 | 3 | |
| Hyperkalaemia | | | |
| subjects affected / exposed | 6 / 93 (6.45%) | 0 / 43 (0.00%) | |
| occurrences (all) | 7 | 0 | |
| Hypocalcaemia | | | |

| | | | |
|-----------------------------|------------------|----------------|--|
| subjects affected / exposed | 2 / 93 (2.15%) | 0 / 43 (0.00%) | |
| occurrences (all) | 3 | 0 | |
| Hypokalaemia | | | |
| subjects affected / exposed | 7 / 93 (7.53%) | 2 / 43 (4.65%) | |
| occurrences (all) | 8 | 2 | |
| Hypomagnesaemia | | | |
| subjects affected / exposed | 11 / 93 (11.83%) | 1 / 43 (2.33%) | |
| occurrences (all) | 12 | 1 | |
| Hyponatraemia | | | |
| subjects affected / exposed | 13 / 93 (13.98%) | 2 / 43 (4.65%) | |
| occurrences (all) | 18 | 2 | |
| Hypophosphataemia | | | |
| subjects affected / exposed | 4 / 93 (4.30%) | 1 / 43 (2.33%) | |
| occurrences (all) | 6 | 1 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|-------------------|---|
| 08 April 2016 | Statistical study design update |
| 27 July 2016 | Inclusion/exclusion criteria update |
| 21 September 2016 | Management Algorithms for Immuno-Oncology Agents update |
| 13 October 2016 | Inclusion/exclusion criteria update |
| 16 February 2017 | Study design simplification and study tracks re-arrangement |
| 12 April 2018 | Study design changes |
| 22 April 2019 | Adjustment of Follow-up period timelines |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

This study was terminated early by sponsor for reasons unrelated to safety..
14 of the 295 participants initially received a treatment and then were re-randomized to a different, non-concomitant second treatment

Notes: