



Clinical trial results:

A Phase II, Open-label, Single-arm, Multicenter Study to Evaluate Efficacy and Safety of Pembrolizumab Monotherapy in Subjects with Advanced Recurrent Ovarian Cancer (KEYNOTE-100)

Summary

| | |
|--------------------------|-------------------------------------|
| EudraCT number | 2015-003338-29 |
| Trial protocol | SE ES LT DE FI NO BE NL FR PL GB IT |
| Global end of trial date | 18 March 2021 |

Results information

| | |
|--------------------------------|---------------|
| Result version number | v1 (current) |
| This version publication date | 13 March 2022 |
| First version publication date | 13 March 2022 |

Trial information

Trial identification

| | |
|-----------------------|----------|
| Sponsor protocol code | 3475-100 |
|-----------------------|----------|

Additional study identifiers

| | |
|------------------------------------|-------------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02674061 |
| WHO universal trial number (UTN) | - |
| Other trial identifiers | JAPIC-CTI: 163237 |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | Merck Sharp & Dohme Corp. |
| Sponsor organisation address | 2000 Galloping Hill Road, Kenilworth, NJ, United States, 07033 |
| Public contact | Clinical Trials Disclosure, Merck Sharp & Dohme Corp., ClinicalTrialsDisclosure@merck.com |
| Scientific contact | Clinical Trials Disclosure, Merck Sharp & Dohme Corp., ClinicalTrialsDisclosure@merck.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 | 18 March 2021 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 18 September 2019 |
| Global end of trial reached? | Yes |
| Global end of trial date | 18 March 2021 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

This study will assess the efficacy and safety of pembrolizumab (MK-3475) monotherapy in female participants with recurrent ovarian cancer (ROC) who have received up to 5 prior lines of treatment including platinum-based treatment for ROC (1 to 6 total prior lines counting front line therapy). Participants will be enrolled into two separate cohorts based on the number of prior lines of treatment received for ROC.

Protection of trial subjects:

This study was conducted in conformance with Good Clinical Practice standards and applicable country and/or local statutes and regulations regarding ethical committee review, informed consent, and the protection of human subjects participating in biomedical research.

Background therapy: -

Evidence for comparator: -

| | |
|---|------------------|
| Actual start date of recruitment | 25 February 2016 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|------------------------|
| Country: Number of subjects enrolled | Australia: 15 |
| Country: Number of subjects enrolled | Belgium: 7 |
| Country: Number of subjects enrolled | Canada: 14 |
| Country: Number of subjects enrolled | Finland: 9 |
| Country: Number of subjects enrolled | France: 21 |
| Country: Number of subjects enrolled | Germany: 22 |
| Country: Number of subjects enrolled | Israel: 29 |
| Country: Number of subjects enrolled | Italy: 44 |
| Country: Number of subjects enrolled | Japan: 21 |
| Country: Number of subjects enrolled | Lithuania: 10 |
| Country: Number of subjects enrolled | Netherlands: 23 |
| Country: Number of subjects enrolled | Norway: 13 |
| Country: Number of subjects enrolled | Poland: 5 |
| Country: Number of subjects enrolled | Russian Federation: 27 |
| Country: Number of subjects enrolled | South Africa: 7 |
| Country: Number of subjects enrolled | Spain: 23 |
| Country: Number of subjects enrolled | Sweden: 5 |
| Country: Number of subjects enrolled | United Kingdom: 17 |

| | |
|--------------------------------------|-------------------|
| Country: Number of subjects enrolled | United States: 64 |
| Worldwide total number of subjects | 376 |
| EEA total number of subjects | 182 |

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) | 236 |
| From 65 to 84 years | 138 |
| 85 years and over | 2 |

Subject disposition

Recruitment

Recruitment details:

Per protocol, Progression-free survival by Blinded Independent Central Review, Overall Survival, adverse events in all participants from end of trial database (cutoff 18-Mar-2021). Objective Response Rate, Duration of Response, Disease Control Rate, safety outcomes, sub-group analyses of PFS and OS from final analysis database (cutoff 18-Sep-2019).

Pre-assignment

Screening details:

Seven participants (Cohorts A=5; B = 2) received a second course of pembrolizumab at the investigator's discretion per protocol. Response/progression or adverse events (AEs) that occurred during second course of pembrolizumab were not counted towards efficacy or safety outcome measures.

Period 1

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

Arms

| | |
|------------------------------|-------------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | Cohort A: Pembrolizumab |

Arm description:

Participants in Cohort A received 0-2 prior lines of treatment for recurrent ovarian cancer (ROC; 1-3 total prior lines including front-line treatment) and were administered pembrolizumab at a dose of 200 mg via intravenous (IV) infusion on Day 1 of each 21-day cycle for up to 35 cycles (up to ~2 years). Qualified participants who complete 35 administrations of pembrolizumab but progress after discontinuation can initiate a second course of pembrolizumab 200 mg for up to 17 cycles (up to ~1 additional year).

| | |
|--|-----------------------|
| Arm type | Experimental |
| Investigational medicinal product name | pembrolizumab |
| Investigational medicinal product code | |
| Other name | MK-3475 KEYTRUDA® |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Administered at a dose of 200 mg via intravenous (IV) infusion on Day 1 of each 21-day cycle

| | |
|------------------|-------------------------|
| Arm title | Cohort B: Pembrolizumab |
|------------------|-------------------------|

Arm description:

Participants in Cohort B received 3-5 prior lines of treatment for ROC (4-6 total prior lines including front-line treatment) and were administered pembrolizumab at a dose of 200 mg via IV infusion on Day 1 of each 21-day cycle for up to 35 cycles (up to ~2 years). Qualified participants who complete 35 administrations of pembrolizumab but progress after discontinuation can initiate a second course of pembrolizumab 200 mg for up to 17 cycles (up to ~1 additional year).

| | |
|--|-----------------------|
| Arm type | Experimental |
| Investigational medicinal product name | pembrolizumab |
| Investigational medicinal product code | |
| Other name | MK-3475 KEYTRUDA® |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Administered at a dose of 200 mg via intravenous (IV) infusion on Day 1 of each 21-day cycle

| Number of subjects in period 1 | Cohort A: Pembrolizumab | Cohort B: Pembrolizumab |
|---|----------------------------|----------------------------|
| Started | 285 | 91 |
| Completed | 0 | 0 |
| Not completed | 285 | 91 |
| Consent withdrawn by subject | 9 | 1 |
| Death | 229 | 77 |
| Participation in study discontinued by Sponsor | 44 | 10 |
| Lost to follow-up | 3 | 3 |

Baseline characteristics

Reporting groups

| | |
|---|-------------------------|
| Reporting group title | Cohort A: Pembrolizumab |
| Reporting group description: | |
| Participants in Cohort A received 0-2 prior lines of treatment for recurrent ovarian cancer (ROC; 1-3 total prior lines including front-line treatment) and were administered pembrolizumab at a dose of 200 mg via intravenous (IV) infusion on Day 1 of each 21-day cycle for up to 35 cycles (up to ~2 years). Qualified participants who complete 35 administrations of pembrolizumab but progress after discontinuation can initiate a second course of pembrolizumab 200 mg for up to 17 cycles (up to ~1 additional year). | |
| Reporting group title | Cohort B: Pembrolizumab |
| Reporting group description: | |
| Participants in Cohort B received 3-5 prior lines of treatment for ROC (4-6 total prior lines including front-line treatment) and were administered pembrolizumab at a dose of 200 mg via IV infusion on Day 1 of each 21-day cycle for up to 35 cycles (up to ~2 years). Qualified participants who complete 35 administrations of pembrolizumab but progress after discontinuation can initiate a second course of pembrolizumab 200 mg for up to 17 cycles (up to ~1 additional year). | |

| Reporting group values | Cohort A: Pembrolizumab | Cohort B: Pembrolizumab | Total |
|---|----------------------------|----------------------------|-------|
| Number of subjects | 285 | 91 | 376 |
| Age categorical Units: Subjects | | | |
| In utero | 0 | 0 | 0 |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | 0 |
| Newborns (0-27 days) | 0 | 0 | 0 |
| Infants and toddlers (28 days-23 months) | 0 | 0 | 0 |
| Children (2-11 years) | 0 | 0 | 0 |
| Adolescents (12-17 years) | 0 | 0 | 0 |
| Adults (18-64 years) | 174 | 62 | 236 |
| From 65-84 years | 109 | 29 | 138 |
| 85 years and over | 2 | 0 | 2 |
| Age Continuous Units: Years | | | |
| arithmetic mean | 60.5 | 59.5 | - |
| standard deviation | ± 11.3 | ± 9.9 | - |
| Sex: Female, Male Units: Participants | | | |
| Female | 285 | 91 | 376 |
| Male | 0 | 0 | 0 |
| Race (NIH/OMB) Units: Subjects | | | |
| American Indian or Alaska Native | 0 | 0 | 0 |
| Asian | 27 | 3 | 30 |
| Native Hawaiian or Other Pacific Islander | 0 | 1 | 1 |
| Black or African American | 4 | 1 | 5 |
| White | 253 | 85 | 338 |
| More than one race | 1 | 0 | 1 |
| Unknown or Not Reported | 0 | 1 | 1 |

| | | | |
|-------------------------|-----|----|-----|
| Ethnicity (NIH/OMB) | | | |
| Units: Subjects | | | |
| Hispanic or Latino | 6 | 3 | 9 |
| Not Hispanic or Latino | 258 | 85 | 343 |
| Unknown or Not Reported | 21 | 3 | 24 |

End points

End points reporting groups

| | |
|-----------------------|-------------------------|
| Reporting group title | Cohort A: Pembrolizumab |
|-----------------------|-------------------------|

Reporting group description:

Participants in Cohort A received 0-2 prior lines of treatment for recurrent ovarian cancer (ROC; 1-3 total prior lines including front-line treatment) and were administered pembrolizumab at a dose of 200 mg via intravenous (IV) infusion on Day 1 of each 21-day cycle for up to 35 cycles (up to ~2 years). Qualified participants who complete 35 administrations of pembrolizumab but progress after discontinuation can initiate a second course of pembrolizumab 200 mg for up to 17 cycles (up to ~1 additional year).

| | |
|-----------------------|-------------------------|
| Reporting group title | Cohort B: Pembrolizumab |
|-----------------------|-------------------------|

Reporting group description:

Participants in Cohort B received 3-5 prior lines of treatment for ROC (4-6 total prior lines including front-line treatment) and were administered pembrolizumab at a dose of 200 mg via IV infusion on Day 1 of each 21-day cycle for up to 35 cycles (up to ~2 years). Qualified participants who complete 35 administrations of pembrolizumab but progress after discontinuation can initiate a second course of pembrolizumab 200 mg for up to 17 cycles (up to ~1 additional year).

| | |
|----------------------------|---|
| Subject analysis set title | Cohort A Participants with PD-L1 CPS ≥ 1 |
|----------------------------|---|

| | |
|---------------------------|--------------------|
| Subject analysis set type | Sub-group analysis |
|---------------------------|--------------------|

Subject analysis set description:

Participants in Cohort A with Programmed Cell Death Ligand-1 (PD-L1) Combined Positive Score (CPS) ≥ 1 received 0-2 prior lines of treatment for recurrent ovarian cancer (ROC; 1-3 total prior lines including front-line treatment) and were administered pembrolizumab at a dose of 200 mg via intravenous (IV) infusion on Day 1 of each 21-day cycle for up to 35 cycles (up to ~2 years). Qualified participants who complete 35 administrations of pembrolizumab but progress after discontinuation can initiate a second course of pembrolizumab 200 mg for up to 17 cycles (up to ~1 additional year).

| | |
|----------------------------|---|
| Subject analysis set title | Cohort B Participants with PD-L1 CPS ≥ 1 |
|----------------------------|---|

| | |
|---------------------------|--------------------|
| Subject analysis set type | Sub-group analysis |
|---------------------------|--------------------|

Subject analysis set description:

Participants in Cohort B with PD-L1 CPS ≥ 1 received 3-5 prior lines of treatment for ROC (4-6 total prior lines including front-line treatment) and were administered pembrolizumab at a dose of 200 mg via IV infusion on Day 1 of each 21-day cycle for up to 35 cycles (up to ~2 years). Qualified participants who complete 35 administrations of pembrolizumab but progress after discontinuation can initiate a second course of pembrolizumab 200 mg for up to 17 cycles (up to ~1 additional year).

| | |
|----------------------------|--|
| Subject analysis set title | Cohort A Participants with PD-L1 CPS ≥ 10 |
|----------------------------|--|

| | |
|---------------------------|--------------------|
| Subject analysis set type | Sub-group analysis |
|---------------------------|--------------------|

Subject analysis set description:

Participants in Cohort A with PD-L1 CPS ≥ 10 received 0-2 prior lines of treatment for recurrent ovarian cancer (ROC; 1-3 total prior lines including front-line treatment) and were administered pembrolizumab at a dose of 200 mg via intravenous (IV) infusion on Day 1 of each 21-day cycle for up to 35 cycles (up to ~2 years). Qualified participants who complete 35 administrations of pembrolizumab but progress after discontinuation can initiate a second course of pembrolizumab 200 mg for up to 17 cycles (up to ~1 additional year).

| | |
|----------------------------|--|
| Subject analysis set title | Cohort B Participants with PD-L1 CPS ≥ 10 |
|----------------------------|--|

| | |
|---------------------------|--------------------|
| Subject analysis set type | Sub-group analysis |
|---------------------------|--------------------|

Subject analysis set description:

Participants in Cohort B with PD-L1 CPS ≥ 10 received 3-5 prior lines of treatment for ROC (4-6 total prior lines including front-line treatment) and were administered pembrolizumab at a dose of 200 mg via IV infusion on Day 1 of each 21-day cycle for up to 35 cycles (up to ~2 years). Qualified participants who complete 35 administrations of pembrolizumab but progress after discontinuation can initiate a second course of pembrolizumab 200 mg for up to 17 cycles (up to ~1 additional year).

| | |
|----------------------------|---|
| Subject analysis set title | Cohort A Participants with PFI/TFI ≥ 3 -6 Months |
|----------------------------|---|

| | |
|---------------------------|--------------------|
| Subject analysis set type | Sub-group analysis |
|---------------------------|--------------------|

Subject analysis set description:

Participants in Cohort A with a platinum-free interval (PFI)/treatment-free interval (TFI) ≥ 3 -6 Months (based on last regimen received) received 0-2 prior lines of treatment for recurrent ovarian cancer (ROC; 1-3 total prior lines including front-line treatment) and were administered pembrolizumab at a dose of 200 mg via intravenous (IV) infusion on Day 1 of each 21-day cycle for up to 35 cycles (up to ~2 years).

~2 years). Qualified participants who complete 35 administrations of pembrolizumab but progress after discontinuation can initiate a second course of pembrolizumab 200 mg for up to 17 cycles (up to ~1 additional year).

| | |
|----------------------------|---|
| Subject analysis set title | Cohort A Participants with PFI/TFI >6-12 Months |
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

Participants in Cohort A with a platinum-free interval (PFI)/treatment-free interval (TFI) >6-12 Months (based on last regimen received) received 0-2 prior lines of treatment for recurrent ovarian cancer (ROC; 1-3 total prior lines including front-line treatment) and were administered pembrolizumab at a dose of 200 mg via intravenous (IV) infusion on Day 1 of each 21-day cycle for up to 35 cycles (up to ~2 years). Qualified participants who complete 35 administrations of pembrolizumab but progress after discontinuation can initiate a second course of pembrolizumab 200 mg for up to 17 cycles (up to ~1 additional year).

Primary: Objective Response Rate (ORR) per Response Evaluation Criteria in Solid Tumors Version 1.1 (RECIST 1.1) by Blinded Independent Central Review (BICR) in all Cohort A and Cohort B Participants

| | |
|-----------------|---|
| End point title | Objective Response Rate (ORR) per Response Evaluation Criteria in Solid Tumors Version 1.1 (RECIST 1.1) by Blinded Independent Central Review (BICR) in all Cohort A and Cohort B Participants ^[1] |
|-----------------|---|

End point description:

ORR was defined as the percentage of participants in the analysis population who had a Complete Response (CR: Disappearance of all target lesions) or a Partial Response (PR: $\geq 30\%$ decrease in the sum of diameters [SOD] of target lesions) using RECIST 1.1 based on BICR. ORR was analyzed by test of binomial parameter and reported as the percentage of participants who experienced CR or PR per RECIST 1.1 by BICR. The analysis population included all participants in Cohort A and Cohort B who received ≥ 1 dose of study drug.

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

End point timeframe:

Up to ~43 months (through database cut-off date of 18-September-2019)

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: There were no statistical analyses planned for this endpoint.

| End point values | Cohort A: Pembrolizumab | Cohort B: Pembrolizumab | | |
|-----------------------------------|----------------------------|----------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 285 | 91 | | |
| Units: Percentage of participants | | | | |
| number (confidence interval 95%) | 8.1 (5.2 to 11.9) | 9.9 (4.6 to 17.9) | | |

Statistical analyses

No statistical analyses for this end point

Primary: ORR per RECIST 1.1 by BICR in Subgroup of Cohort A and Cohort B Participants with Programmed Cell Death Ligand-1 (PD-L1) Combined Positive Score (CPS) ≥ 10

| | |
|-----------------|---|
| End point title | ORR per RECIST 1.1 by BICR in Subgroup of Cohort A and Cohort B Participants with Programmed Cell Death Ligand-1 (PD-L1) Combined Positive Score (CPS) ≥ 10 ^[2] |
|-----------------|---|

End point description:

ORR was defined as the percentage of participants in the analysis population who had a CR

(Disappearance of all target lesions) or a PR ($\geq 30\%$ decrease in SOD of target lesions) using RECIST 1.1 based on BICR. ORR was analyzed by test of binomial parameter and reported as the percentage of participants who experienced CR or PR per RECIST 1.1 by BICR. The analysis population included a subgroup of participants in Cohort A and Cohort B who had a PD-L1 biomarker positive expression defined by immunohistochemistry (IHC) as CPS ≥ 10 and received ≥ 1 dose of study drug.

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

End point timeframe:

Up to ~43 months (through database cut-off date of 18-September-2019)

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: There were no statistical analyses planned for this endpoint.

| End point values | Cohort A Participants with PD-L1 CPS ≥ 10 | Cohort B Participants with PD-L1 CPS ≥ 10 | | |
|-----------------------------------|---|---|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 43 | 22 | | |
| Units: Percentage of participants | | | | |
| number (confidence interval 95%) | 11.6 (3.9 to 25.1) | 18.2 (5.2 to 40.3) | | |

Statistical analyses

No statistical analyses for this end point

Primary: ORR per RECIST 1.1 by BICR in Subgroup of Cohort A and Cohort B Participants with PD-L1 CPS ≥ 1

| | |
|-----------------|---|
| End point title | ORR per RECIST 1.1 by BICR in Subgroup of Cohort A and Cohort B Participants with PD-L1 CPS ≥ 1 ^[3] |
|-----------------|---|

End point description:

ORR was defined as the percentage of participants in the analysis population who had a CR (Disappearance of all target lesions) or a PR ($\geq 30\%$ decrease in SOD of target lesions) using RECIST 1.1 based on BICR. ORR was analyzed by test of binomial parameter and reported as the percentage of participants who experienced CR or PR per RECIST 1.1 by BICR. The analysis population included a subgroup of participants in Cohort A and Cohort B who had a PD-L1 biomarker positive expression defined by IHC as CPS ≥ 1 and received ≥ 1 dose of study drug.

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

End point timeframe:

Up to ~43 months (through database cut-off date of 18-September-2019)

Notes:

[3] - 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: There were no statistical analyses planned for this endpoint.

| End point values | Cohort A Participants with PD-L1 CPS ≥ 1 | Cohort B Participants with PD-L1 CPS ≥ 1 | | |
|-----------------------------------|--|--|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 101 | 49 | | |
| Units: Percentage of participants | | | | |
| number (confidence interval 95%) | 6.9 (2.8 to 13.8) | 10.2 (3.4 to 22.2) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (DOR) per RECIST 1.1 by BICR in all Cohort A and Cohort B Participants

| | |
|-----------------|---|
| End point title | Duration of Response (DOR) per RECIST 1.1 by BICR in all Cohort A and Cohort B Participants |
|-----------------|---|

End point description:

For participants who demonstrated a confirmed CR (disappearance of all target lesions) or PR ($\geq 30\%$ decrease in SOD of target lesions) per RECIST 1.1 based on BICR, DOR was defined as time from first documented CR or PR until progressive disease (PD) or death, whichever occurs first. DOR for participants who didn't progress or die at time of analysis was censored at last tumor assessment. Per RECIST 1.1 PD is a $\geq 20\%$ increase in target lesion SOD and absolute SOD increase of ≥ 5 mm. Appearance of ≥ 1 new lesion is also PD. DOR was analyzed by Kaplan-Meier (KM) method and reported as Median DOR with a full range. The analysis population included all participants in Cohort A and Cohort B who had a confirmed CR or PR per RECIST 1.1 by BICR and received ≥ 1 dose of study drug.

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

End point timeframe:

Up to ~43 months (through database cut-off date of 18-September-2019)

| End point values | Cohort A: Pembrolizumab | Cohort B: Pembrolizumab | | |
|-------------------------------|----------------------------|----------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 23 | 9 | | |
| Units: Months | | | | |
| median (full range (min-max)) | 8.3 (3.9 to 35.4) | 23.6 (3.3 to 32.8) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: DOR per RECIST 1.1 by BICR in Subgroup of Cohort A and Cohort B Participants with PD-L1 CPS ≥ 10

| | |
|-----------------|---|
| End point title | DOR per RECIST 1.1 by BICR in Subgroup of Cohort A and Cohort B Participants with PD-L1 CPS ≥ 10 |
|-----------------|---|

End point description:

For participants who demonstrated a confirmed CR (disappearance of all target lesions) or PR ($\geq 30\%$ decrease in SOD of target lesions) per RECIST 1.1 based on BICR, DOR was defined as time from first documented CR or PR until PD or death, whichever occurs first. DOR for participants who didn't progress or die at time of analysis was censored at last tumor assessment. Per RECIST 1.1 PD was defined as $\geq 20\%$ increase in target lesion SOD and absolute SOD increase of ≥ 5 mm. Appearance of ≥ 1 new lesion is also PD. DOR was analyzed by KM method and reported as Median DOR with a full range. A value of 9999=Median and upper limit not reached at time of data cut-off due to insufficient number of

responding participants with relapse. The analysis population included a subgroup of participants in Cohort A and Cohort B who had a PD-L1 biomarker positive expression defined by IHC as CPS ≥ 10 , had a confirmed CR or PR per RECIST 1.1 by BICR, and received ≥ 1 dose of study drug.

| | |
|---|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Up to ~43 months (through database cut-off date of 18-September-2019) | |

| End point values | Cohort A Participants with PD-L1 CPS ≥ 10 | Cohort B Participants with PD-L1 CPS ≥ 10 | | |
|-------------------------------|---|---|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 5 | 4 | | |
| Units: Months | | | | |
| median (full range (min-max)) | 11.1 (8.3 to 20.5) | 9999 (5.9 to 9999) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: DOR per RECIST 1.1 by BICR in Subgroup of Cohort A and Cohort B Participants with PD-L1 CPS ≥ 1

| | |
|-----------------|--|
| End point title | DOR per RECIST 1.1 by BICR in Subgroup of Cohort A and Cohort B Participants with PD-L1 CPS ≥ 1 |
|-----------------|--|

End point description:

For participants who demonstrated a confirmed CR (disappearance of all target lesions) or PR ($\geq 30\%$ decrease in SOD of target lesions) per RECIST 1.1 based on BICR, DOR was defined as time from first documented CR or PR until PD or death, whichever occurs first. DOR for participants who didn't progress or die at time of analysis was censored at last tumor assessment. Per RECIST 1.1 PD was defined as $\geq 20\%$ increase in target lesion SOD and absolute SOD increase of ≥ 5 mm. Appearance of ≥ 1 new lesion is also PD. DOR was analyzed by KM method and reported as Median DOR with a full range. A value of 9999=Median and upper limit not reached at time of data cut-off due to insufficient number of responding participants with relapse. The analysis population included a subgroup of participants in Cohort A and Cohort B who had a PD-L1 biomarker positive expression defined by IHC as CPS ≥ 1 , had a confirmed CR or PR per RECIST 1.1 by BICR, and received ≥ 1 dose of study drug.

| | |
|---|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Up to ~43 months (through database cut-off date of 18-September-2019) | |

| End point values | Cohort A Participants with PD-L1 CPS ≥ 1 | Cohort B Participants with PD-L1 CPS ≥ 1 | | |
|-------------------------------|--|--|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 7 | 5 | | |
| Units: Months | | | | |
| median (full range (min-max)) | 11.1 (8.2 to 35.4) | 9999 (5.9 to 9999) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Disease Control Rate (DCR) per RECIST 1.1 by BICR in all Cohort A and Cohort B Participants

| | |
|-----------------|---|
| End point title | Disease Control Rate (DCR) per RECIST 1.1 by BICR in all Cohort A and Cohort B Participants |
|-----------------|---|

End point description:

DCR was defined as the percentage of participants in the analysis population who had a CR (Disappearance of all target lesions) or PR ($\geq 30\%$ decrease in SOD of target lesions) or Stable Disease (SD: Neither sufficient shrinkage for PR nor sufficient increase for PD [at $\geq 20\%$ increase in target lesion SOD and absolute SOD increase of ≥ 5 mm. Appearance of ≥ 1 new lesion is also PD]) or Non-CR/Non-PD (NN: does not qualify for CR or PD) for ≥ 24 weeks per RECIST 1.1 based on BICR. DCR was analyzed by test of binomial parameter and reported as the percentage of participants who experienced CR, PR, SD or NN per RECIST 1.1 by BICR. The analysis population included all participants in Cohort A and Cohort B who received ≥ 1 dose of study drug.

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

End point timeframe:

Up to ~43 months (through database cut-off date of 18-September-2019)

| End point values | Cohort A: Pembrolizumab | Cohort B: Pembrolizumab | | |
|-----------------------------------|----------------------------|----------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 285 | 91 | | |
| Units: Percentage of Participants | | | | |
| number (confidence interval 95%) | 22.1 (17.4 to 27.4) | 22.0 (14.0 to 31.9) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: DCR per RECIST 1.1 by BICR in Subgroup of Cohort A and Cohort B Participants with PD-L1 CPS ≥ 10

| | |
|-----------------|---|
| End point title | DCR per RECIST 1.1 by BICR in Subgroup of Cohort A and Cohort B Participants with PD-L1 CPS ≥ 10 |
|-----------------|---|

End point description:

DCR was defined as the percentage of participants in the analysis population who had a CR (Disappearance of all target lesions) or PR ($\geq 30\%$ decrease in SOD of target lesions) or SD (Neither sufficient shrinkage for PR nor sufficient increase for PD [at $\geq 20\%$ increase in target lesion SOD and absolute SOD increase of ≥ 5 mm. Appearance of ≥ 1 new lesion is also PD]) or NN (does not qualify for CR or PD) for ≥ 24 weeks per RECIST 1.1 based on BICR. DCR was analyzed by test of binomial parameter and reported as the percentage of participants who experienced CR, PR, SD or NN per RECIST 1.1 by BICR. The analysis population included a subgroup of participants in Cohort A and Cohort

B who had a PD-L1 biomarker positive expression defined by IHC as CPS ≥ 10 and received ≥ 1 dose of study drug.

| | |
|---|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Up to ~43 months (through database cut-off date of 18-September-2019) | |

| End point values | Cohort A Participants with PD-L1 CPS ≥ 10 | Cohort B Participants with PD-L1 CPS ≥ 10 | | |
|-----------------------------------|---|---|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 43 | 22 | | |
| Units: Percentage of Participants | | | | |
| number (confidence interval 95%) | 25.6 (13.5 to 41.2) | 31.8 (13.9 to 54.9) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: DCR per RECIST 1.1 by BICR in Subgroup of Cohort A and Cohort B Participants with PD-L1 CPS ≥ 1

| | |
|-----------------|--|
| End point title | DCR per RECIST 1.1 by BICR in Subgroup of Cohort A and Cohort B Participants with PD-L1 CPS ≥ 1 |
|-----------------|--|

End point description:

DCR was defined as the percentage of participants in the analysis population who had a CR (Disappearance of all target lesions) or PR ($\geq 30\%$ decrease in SOD of target lesions) or SD (Neither sufficient shrinkage for PR nor sufficient increase for PD [at $\geq 20\%$ increase in target lesion SOD and absolute SOD increase of ≥ 5 mm. Appearance of ≥ 1 new lesion is also PD]) or NN (does not qualify for CR or PD) for ≥ 24 weeks per RECIST 1.1 based on BICR. DCR was analyzed by test of binomial parameter and reported as the percentage of participants who experienced CR, PR, SD or NN per RECIST 1.1 by BICR. The analysis population included a subgroup of participants in Cohort A and Cohort B who had a PD-L1 biomarker positive expression defined by IHC as CPS ≥ 1 and received ≥ 1 dose of study drug.

| | |
|---|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Up to ~43 months (through database cut-off date of 18-September-2019) | |

| End point values | Cohort A Participants with PD-L1 CPS ≥ 1 | Cohort B Participants with PD-L1 CPS ≥ 1 | | |
|-----------------------------------|--|--|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 101 | 49 | | |
| Units: Percentage of participants | | | | |
| number (confidence interval 95%) | 24.8 (16.7 to 34.3) | 22.4 (11.8 to 36.6) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Progression Free Survival (PFS) per RECIST 1.1 by BICR in all Cohort A and Cohort B Participants

| | |
|-----------------|--|
| End point title | Progression Free Survival (PFS) per RECIST 1.1 by BICR in all Cohort A and Cohort B Participants |
|-----------------|--|

End point description:

PFS was defined as the time from first dose of study treatment to the first documented PD per RECIST 1.1 based on BICR, or death due to any cause, whichever occurred first. Per RECIST 1.1 PD was defined as $\geq 20\%$ increase in SOD of target lesions and an absolute SOD increase of ≥ 5 mm. The appearance of ≥ 1 new lesion is also PD. PFS was analyzed by KM method and reported as Median PFS per RECIST 1.1 by BICR with a 95% confidence interval (CI). The analysis population included all participants in Cohort A and Cohort B who received ≥ 1 dose of study drug.

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

End point timeframe:

Up to ~58.8 months (through database cut-off date of 18-March-2021)

| End point values | Cohort A: Pembrolizumab | Cohort B: Pembrolizumab | | |
|----------------------------------|----------------------------|----------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 285 | 91 | | |
| Units: Months | | | | |
| median (confidence interval 95%) | 2.1 (2.1 to 2.2) | 2.1 (2.1 to 2.6) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with PFS (PFS Rate) at Month 6 per RECIST 1.1 by BICR in all Cohort A and Cohort B Participants

| | |
|-----------------|--|
| End point title | Percentage of Participants with PFS (PFS Rate) at Month 6 per RECIST 1.1 by BICR in all Cohort A and Cohort B Participants |
|-----------------|--|

End point description:

PFS was defined as the time from first dose of study treatment to the first documented PD per RECIST 1.1 based on BICR, or death due to any cause, whichever occurred first. Per RECIST 1.1 PD was defined as $\geq 20\%$ increase in SOD of target lesions and an absolute SOD increase of ≥ 5 mm. The appearance of ≥ 1 new lesion is also PD. The percentage of participants with PFS (PFS rate) at Month 6 per RECIST 1.1 by BICR is reported. The analysis population included all participants in Cohort A and Cohort B who received ≥ 1 dose of study drug.

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

End point timeframe:

Month 6

| End point values | Cohort A: Pembrolizumab | Cohort B: Pembrolizumab | | |
|-----------------------------------|----------------------------|----------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 285 | 91 | | |
| Units: Percentage of Participants | | | | |
| number (confidence interval 95%) | 23.0 (18.1 to 28.1) | 27.2 (18.2 to 36.9) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with PFS (PFS Rate) at Month 18 per RECIST 1.1 by BICR in all Cohort A and Cohort B Participants

| | |
|-----------------|---|
| End point title | Percentage of Participants with PFS (PFS Rate) at Month 18 per RECIST 1.1 by BICR in all Cohort A and Cohort B Participants |
|-----------------|---|

End point description:

PFS was defined as the time from first dose of study treatment to the first documented PD per RECIST 1.1 based on BICR, or death due to any cause, whichever occurred first. Per RECIST 1.1 PD was defined as $\geq 20\%$ increase in SOD of target lesions and an absolute SOD increase of ≥ 5 mm. The appearance of ≥ 1 new lesion is also PD. The percentage of participants with PFS (PFS rate) at Month 18 per RECIST 1.1 by BICR is reported. The analysis population included all participants in Cohort A and Cohort B who received ≥ 1 dose of study drug.

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

End point timeframe:

Month 18

| End point values | Cohort A: Pembrolizumab | Cohort B: Pembrolizumab | | |
|-----------------------------------|----------------------------|----------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 285 | 91 | | |
| Units: Percentage of Participants | | | | |
| number (confidence interval 95%) | 5.8 (3.2 to 9.5) | 13.1 (6.5 to 22.2) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with PFS (PFS Rate) at Month 12 per RECIST 1.1 by BICR in all Cohort A and Cohort B Participants

| | |
|-----------------|---|
| End point title | Percentage of Participants with PFS (PFS Rate) at Month 12 per RECIST 1.1 by BICR in all Cohort A and Cohort B Participants |
|-----------------|---|

End point description:

PFS was defined as the time from first dose of study treatment to the first documented PD per RECIST 1.1 based on BICR, or death due to any cause, whichever occurred first. Per RECIST 1.1 PD was defined as $\geq 20\%$ increase in SOD of target lesions and an absolute SOD increase of ≥ 5 mm. The appearance of ≥ 1 new lesion is also PD. The percentage of participants with PFS (PFS rate) at Month 12 per RECIST 1.1 by BICR is reported. The analysis population included all participants in Cohort A and Cohort B who received ≥ 1 dose of study drug.

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

End point timeframe:

Month 12

| End point values | Cohort A: Pembrolizumab | Cohort B: Pembrolizumab | | |
|-----------------------------------|----------------------------|----------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 285 | 91 | | |
| Units: Percentage of Participants | | | | |
| number (confidence interval 95%) | 10.5 (7.0 to 14.8) | 13.1 (6.5 to 22.2) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: PFS per RECIST 1.1 by BICR in Subgroup of Cohort A and Cohort B Participants with PD-L1 CPS ≥ 10

| | |
|-----------------|---|
| End point title | PFS per RECIST 1.1 by BICR in Subgroup of Cohort A and Cohort B Participants with PD-L1 CPS ≥ 10 |
|-----------------|---|

End point description:

PFS was defined as the time from first dose of study treatment to the first documented PD per RECIST 1.1 based on BICR, or death due to any cause, whichever occurred first. Per RECIST 1.1 PD was defined as $\geq 20\%$ increase in SOD of target lesions and an absolute SOD increase of ≥ 5 mm. The appearance of ≥ 1 new lesion is also PD. PFS was analyzed by KM method and reported as Median PFS per RECIST 1.1 by BICR with a 95% CI. The analysis population included a subgroup of participants in Cohort A and Cohort B who had a PD-L1 biomarker positive expression defined by IHC as CPS ≥ 10 and received ≥ 1 dose of study drug.

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

End point timeframe:

Up to ~43 months (through database cut-off date of 18-September-2019)

| End point values | Cohort A Participants with PD-L1 CPS ≥ 10 | Cohort B Participants with PD-L1 CPS ≥ 10 | | |
|----------------------------------|---|---|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 43 | 22 | | |
| Units: Months | | | | |
| median (confidence interval 95%) | 2.1 (2.1 to 4.2) | 2.1 (2.0 to 8.3) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with PFS (PFS Rate) at Month 6 per RECIST 1.1 by BICR in Subgroup of Cohort A and Cohort B Participants with PD-L1 CPS ≥ 10

| | |
|-----------------|---|
| End point title | Percentage of Participants with PFS (PFS Rate) at Month 6 per RECIST 1.1 by BICR in Subgroup of Cohort A and Cohort B Participants with PD-L1 CPS ≥ 10 |
|-----------------|---|

End point description:

PFS was defined as the time from first dose of study treatment to the first documented PD per RECIST 1.1 based on BICR, or death due to any cause, whichever occurred first. Per RECIST 1.1 PD was defined as $\geq 20\%$ increase in SOD of target lesions and an absolute SOD increase of ≥ 5 mm. The appearance of ≥ 1 new lesion is also PD. The percentage of participants with PFS (PFS rate) at Month 6 per RECIST 1.1 by BICR is reported. The analysis population included a subgroup of participants in Cohort A and Cohort B who had a PD-L1 biomarker positive expression defined by IHC as CPS ≥ 10 and received ≥ 1 dose of study drug.

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

End point timeframe:

Month 6

| End point values | Cohort A Participants with PD-L1 CPS ≥ 10 | Cohort B Participants with PD-L1 CPS ≥ 10 | | |
|-----------------------------------|---|---|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 43 | 22 | | |
| Units: Percentage of Participants | | | | |
| number (confidence interval 95%) | 26.9 (14.4 to 41.2) | 36.8 (17.0 to 57.0) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with PFS (PFS Rate) at Month 12 per RECIST 1.1 by BICR in Subgroup of Cohort A and Cohort B Participants with PD-L1 CPS ≥ 10

| | |
|-----------------|--|
| End point title | Percentage of Participants with PFS (PFS Rate) at Month 12 per RECIST 1.1 by BICR in Subgroup of Cohort A and Cohort B Participants with PD-L1 CPS ≥ 10 |
|-----------------|--|

End point description:

PFS was defined as the time from first dose of study treatment to the first documented PD per RECIST 1.1 based on BICR, or death due to any cause, whichever occurred first. Per RECIST 1.1 PD was defined as $\geq 20\%$ increase in SOD of target lesions and an absolute SOD increase of ≥ 5 mm. The appearance of ≥ 1 new lesion is also PD. The percentage of participants with PFS (PFS rate) at Month 12 per RECIST

1.1 by BICR is reported. The analysis population included a subgroup of participants in Cohort A and Cohort B who had a PD-L1 biomarker positive expression defined by IHC as CPS ≥ 10 and received ≥ 1 dose of study drug.

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Month 12 | |

| End point values | Cohort A Participants with PD-L1 CPS ≥ 10 | Cohort B Participants with PD-L1 CPS ≥ 10 | | |
|-----------------------------------|---|---|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 43 | 22 | | |
| Units: Percentage of Participants | | | | |
| number (confidence interval 95%) | 18.2 (7.9 to 31.9) | 16.8 (3.5 to 38.7) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with PFS (PFS Rate) at Month 18 per RECIST 1.1 by BICR in Subgroup of Cohort A and Cohort B Participants with PD-L1 CPS ≥ 10

| | |
|-----------------|--|
| End point title | Percentage of Participants with PFS (PFS Rate) at Month 18 per RECIST 1.1 by BICR in Subgroup of Cohort A and Cohort B Participants with PD-L1 CPS ≥ 10 |
|-----------------|--|

End point description:

PFS was defined as the time from first dose of study treatment to the first documented PD per RECIST 1.1 based on BICR, or death due to any cause, whichever occurred first. Per RECIST 1.1 PD was defined as $\geq 20\%$ increase in SOD of target lesions and an absolute SOD increase of ≥ 5 mm. The appearance of ≥ 1 new lesion is also PD. The percentage of participants with PFS (PFS rate) at Month 18 per RECIST 1.1 by BICR is reported. The analysis population included a subgroup of participants in Cohort A and Cohort B who had a PD-L1 biomarker positive expression defined by IHC as CPS ≥ 10 and received ≥ 1 dose of study drug.

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Month 18 | |

| End point values | Cohort A Participants with PD-L1 CPS ≥ 10 | Cohort B Participants with PD-L1 CPS ≥ 10 | | |
|-----------------------------------|---|---|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 43 | 22 | | |
| Units: Percentage of Participants | | | | |
| number (confidence interval 95%) | 9.1 (2.4 to 21.3) | 16.8 (3.5 to 38.7) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: PFS per RECIST 1.1 by BICR in Subgroup of Cohort A and Cohort B Participants with PD-L1 CPS ≥ 1

| | |
|-----------------|--|
| End point title | PFS per RECIST 1.1 by BICR in Subgroup of Cohort A and Cohort B Participants with PD-L1 CPS ≥ 1 |
|-----------------|--|

End point description:

PFS was defined as the time from first dose of study treatment to the first documented PD per RECIST 1.1 based on BICR, or death due to any cause, whichever occurred first. Per RECIST 1.1 PD was defined as $\geq 20\%$ increase in SOD of target lesions and an absolute SOD increase of ≥ 5 mm. The appearance of ≥ 1 new lesion is also PD. PFS was analyzed by KM method and reported as Median PFS per RECIST 1.1 by BICR with a 95% CI. The analysis population included a subgroup of participants in Cohort A and Cohort B who had a PD-L1 biomarker positive expression defined by IHC as CPS ≥ 1 and received ≥ 1 dose of study drug.

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

End point timeframe:

Up to ~43 months (through database cut-off date of 18-September-2019)

| End point values | Cohort A Participants with PD-L1 CPS ≥ 1 | Cohort B Participants with PD-L1 CPS ≥ 1 | | |
|----------------------------------|--|--|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 101 | 49 | | |
| Units: Months | | | | |
| median (confidence interval 95%) | 2.1 (2.1 to 2.8) | 2.1 (2.1 to 3.3) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with PFS (PFS Rate) at Month 6 per RECIST 1.1 by BICR in Subgroup of Cohort A and Cohort B Participants with PD-L1 CPS ≥ 1

| | |
|-----------------|--|
| End point title | Percentage of Participants with PFS (PFS Rate) at Month 6 per RECIST 1.1 by BICR in Subgroup of Cohort A and Cohort B Participants with PD-L1 CPS ≥ 1 |
|-----------------|--|

End point description:

PFS was defined as the time from first dose of study treatment to the first documented PD per RECIST 1.1 based on BICR, or death due to any cause, whichever occurred first. Per RECIST 1.1 PD was defined as $\geq 20\%$ increase in SOD of target lesions and an absolute SOD increase of ≥ 5 mm. The appearance of ≥ 1 new lesion is also PD. The percentage of participants with PFS (PFS rate) at Month 6 per RECIST 1.1 by BICR is reported. The analysis population included a subgroup of participants in Cohort A and Cohort B who had a PD-L1 biomarker positive expression defined by IHC as CPS ≥ 1 and received ≥ 1 dose of

study drug.

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Month 6 | |

| End point values | Cohort A Participants with PD-L1 CPS ≥1 | Cohort B Participants with PD-L1 CPS ≥1 | | |
|-----------------------------------|--|--|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 101 | 49 | | |
| Units: Percentage of Participants | | | | |
| number (confidence interval 95%) | 25.5 (17.2 to 34.5) | 25.6 (14.1 to 38.8) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with PFS (PFS Rate) at Month 12 per RECIST 1.1 by BICR in Subgroup of Cohort A and Cohort B Participants with PD-L1 CPS ≥1

| | |
|-----------------|---|
| End point title | Percentage of Participants with PFS (PFS Rate) at Month 12 per RECIST 1.1 by BICR in Subgroup of Cohort A and Cohort B Participants with PD-L1 CPS ≥1 |
|-----------------|---|

End point description:

PFS was defined as the time from first dose of study treatment to the first documented PD per RECIST 1.1 based on BICR, or death due to any cause, whichever occurred first. Per RECIST 1.1 PD was defined as ≥20% increase in SOD of target lesions and an absolute SOD increase of ≥5 mm. The appearance of ≥1 new lesion is also PD. The percentage of participants with PFS (PFS rate) at Month 12 per RECIST 1.1 by BICR is reported. The analysis population included a subgroup of participants in Cohort A and Cohort B who had a PD-L1 biomarker positive expression defined by IHC as CPS ≥1 and received ≥1 dose of study drug.

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Month 12 | |

| End point values | Cohort A Participants with PD-L1 CPS ≥1 | Cohort B Participants with PD-L1 CPS ≥1 | | |
|-----------------------------------|--|--|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 101 | 49 | | |
| Units: Percentage of Participants | | | | |
| number (confidence interval 95%) | 16.4 (9.5 to 25.0) | 11.6 (3.8 to 24.4) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with PFS (PFS Rate) at Month 18 per RECIST 1.1 by BICR in Subgroup of Cohort A and Cohort B Participants with PD-L1 CPS ≥ 1

| | |
|-----------------|---|
| End point title | Percentage of Participants with PFS (PFS Rate) at Month 18 per RECIST 1.1 by BICR in Subgroup of Cohort A and Cohort B Participants with PD-L1 CPS ≥ 1 |
|-----------------|---|

End point description:

PFS was defined as the time from first dose of study treatment to the first documented PD per RECIST 1.1 based on BICR, or death due to any cause, whichever occurred first. Per RECIST 1.1 PD was defined as $\geq 20\%$ increase in SOD of target lesions and an absolute SOD increase of ≥ 5 mm. The appearance of ≥ 1 new lesion is also PD. The percentage of participants with PFS (PFS rate) at Month 18 per RECIST 1.1 by BICR is reported. The analysis population included a subgroup of participants in Cohort A and Cohort B who had a PD-L1 biomarker positive expression defined by IHC as CPS ≥ 1 and received ≥ 1 dose of study drug.

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

End point timeframe:

Month 18

| End point values | Cohort A Participants with PD-L1 CPS ≥ 1 | Cohort B Participants with PD-L1 CPS ≥ 1 | | |
|-----------------------------------|--|--|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 101 | 49 | | |
| Units: Percentage of Participants | | | | |
| number (confidence interval 95%) | 9.0 (3.9 to 16.7) | 11.6 (3.8 to 24.4) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: ORR per RECIST 1.1 by Investigator in all Cohort A and Cohort B Participants

| | |
|-----------------|--|
| End point title | ORR per RECIST 1.1 by Investigator in all Cohort A and Cohort B Participants |
|-----------------|--|

End point description:

ORR was defined as the percentage of participants in the analysis population who had a CR (Disappearance of all target lesions) or a PR ($\geq 30\%$ decrease in SOD of target lesions) using RECIST 1.1 based on investigator assessment. ORR was analyzed by test of binomial parameter and reported as the percentage of participants who experienced CR or PR per RECIST 1.1 by investigator. The analysis population included all participants in Cohort A and Cohort B that received ≥ 1 dose of study drug.

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

End point timeframe:

Up to ~43 months (through database cut-off date of 18-September-2019)

| End point values | Cohort A: Pembrolizumab | Cohort B: Pembrolizumab | | |
|-----------------------------------|----------------------------|----------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 285 | 91 | | |
| Units: Percentage of participants | | | | |
| number (confidence interval 95%) | 7.0 (4.3 to 10.6) | 8.8 (3.9 to 16.6) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: ORR per RECIST 1.1 by Investigator in Subgroup of Cohort A and Cohort B Participants with PD-L1 CPS ≥ 10

| | |
|-----------------|---|
| End point title | ORR per RECIST 1.1 by Investigator in Subgroup of Cohort A and Cohort B Participants with PD-L1 CPS ≥ 10 |
|-----------------|---|

End point description:

ORR was defined as the percentage of participants in the analysis population who had a CR (Disappearance of all target lesions) or a PR ($\geq 30\%$ decrease in SOD of target lesions) using RECIST 1.1 based on investigator assessment. ORR was analyzed by test of binomial parameter and reported as the percentage of participants who experienced CR or PR per RECIST 1.1 by investigator. The analysis population included a subgroup of participants in Cohort A and Cohort B who had a PD-L1 biomarker positive expression defined by IHC as CPS ≥ 10 and received ≥ 1 dose of study drug.

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

End point timeframe:

Up to ~43 months (through database cut-off date of 18-September-2019)

| End point values | Cohort A Participants with PD-L1 CPS ≥ 10 | Cohort B Participants with PD-L1 CPS ≥ 10 | | |
|-----------------------------------|---|---|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 43 | 22 | | |
| Units: Percentage of participants | | | | |
| number (confidence interval 95%) | 11.6 (3.9 to 25.1) | 18.2 (5.2 to 40.3) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: ORR per RECIST 1.1 by Investigator in Subgroup of Cohort A and Cohort B Participants with PD-L1 CPS ≥ 1

| | |
|-----------------|--|
| End point title | ORR per RECIST 1.1 by Investigator in Subgroup of Cohort A and Cohort B Participants with PD-L1 CPS ≥ 1 |
|-----------------|--|

End point description:

ORR was defined as the percentage of participants in the analysis population who had a CR (Disappearance of all target lesions) or a PR ($\geq 30\%$ decrease in SOD of target lesions) using RECIST 1.1 based on investigator assessment. ORR was analyzed by test of binomial parameter and reported as the

percentage of participants who experienced CR or PR per RECIST 1.1 by investigator. The analysis population included a subgroup of participants in Cohort A and Cohort B who had a PD-L1 biomarker positive expression defined by IHC as CPS ≥ 1 and received ≥ 1 dose of study drug.

| | |
|---|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Up to ~43 months (through database cut-off date of 18-September-2019) | |

| End point values | Cohort A Participants with PD-L1 CPS ≥ 1 | Cohort B Participants with PD-L1 CPS ≥ 1 | | |
|-----------------------------------|--|--|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 101 | 49 | | |
| Units: Percentage of participants | | | | |
| number (confidence interval 95%) | 6.9 (2.8 to 13.8) | 12.2 (4.6 to 24.8) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: DOR per RECIST 1.1 by Investigator in all Cohort A and Cohort B Participants

| | |
|-----------------|--|
| End point title | DOR per RECIST 1.1 by Investigator in all Cohort A and Cohort B Participants |
|-----------------|--|

End point description:

For participants who demonstrated a confirmed CR (disappearance of all target lesions) or PR ($\geq 30\%$ decrease in SOD of target lesions) per RECIST 1.1 by investigator assessment, DOR was defined as time from first documented CR or PR until PD or death, whichever occurs first. DOR for participants who didn't progress or die at time of analysis was censored at last tumor assessment. Per RECIST 1.1 PD is a $\geq 20\%$ increase in target lesion SOD and absolute SOD increase of ≥ 5 mm. Appearance of ≥ 1 new lesion is also PD. DOR was analyzed by KM method and reported as Median DOR with a full range. The analysis population included all participants in Cohort A and Cohort B who had a confirmed CR or PR per RECIST 1.1 by investigator and received ≥ 1 dose of study drug.

| | |
|---|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Up to ~43 months (through database cut-off date of 18-September-2019) | |

| End point values | Cohort A: Pembrolizumab | Cohort B: Pembrolizumab | | |
|-------------------------------|----------------------------|----------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 20 | 8 | | |
| Units: Months | | | | |
| median (full range (min-max)) | 9.1 (4.0 to 35.4) | 7.5 (4.2 to 32.9) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: DOR per RECIST 1.1 by Investigator in Subgroup of Cohort A and Cohort B Participants with PD-L1 CPS ≥ 10

| | |
|-----------------|---|
| End point title | DOR per RECIST 1.1 by Investigator in Subgroup of Cohort A and Cohort B Participants with PD-L1 CPS ≥ 10 |
|-----------------|---|

End point description:

For participants who demonstrated a confirmed CR (disappearance of all target lesions) or PR ($\geq 30\%$ decrease in SOD of target lesions) per RECIST 1.1 by investigator assessment, DOR was defined as time from first documented CR or PR until PD or death, whichever occurs first. DOR for participants who didn't progress or die at time of analysis was censored at last tumor assessment. Per RECIST 1.1 PD was defined as $\geq 20\%$ increase in target lesion SOD and absolute SOD increase of ≥ 5 mm. Appearance of ≥ 1 new lesion is also PD. DOR was analyzed by KM method and reported as Median DOR with a full range. The analysis population included a subgroup of participants in Cohort A and Cohort B who had a PD-L1 biomarker positive expression defined by IHC as CPS ≥ 10 , had a confirmed CR or PR per RECIST 1.1 by investigator, and received ≥ 1 dose of study drug.

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

End point timeframe:

Up to ~43 months (through database cut-off date of 18-September-2019)

| End point values | Cohort A Participants with PD-L1 CPS ≥ 10 | Cohort B Participants with PD-L1 CPS ≥ 10 | | |
|-------------------------------|---|---|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 5 | 4 | | |
| Units: Months | | | | |
| median (full range (min-max)) | 9.8 (4.0 to 22.6) | 7.3 (4.2 to 32.9) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: DOR per RECIST 1.1 by Investigator in Subgroup of Cohort A and Cohort B Participants with PD-L1 CPS ≥ 1

| | |
|-----------------|--|
| End point title | DOR per RECIST 1.1 by Investigator in Subgroup of Cohort A and Cohort B Participants with PD-L1 CPS ≥ 1 |
|-----------------|--|

End point description:

For participants who demonstrated a confirmed CR (disappearance of all target lesions) or PR ($\geq 30\%$ decrease in SOD of target lesions) per RECIST 1.1 by investigator assessment, DOR was defined as time from first documented CR or PR until PD or death, whichever occurs first. DOR for participants who didn't progress or die at time of analysis was censored at last tumor assessment. Per RECIST 1.1 PD was defined as $\geq 20\%$ increase in target lesion SOD and absolute SOD increase of ≥ 5 mm. Appearance of ≥ 1 new lesion is also PD. DOR analyzed by KM method and reported as Median DOR with a full range. The analysis population included a subgroup of participants in Cohort A and Cohort B who had a PD-L1 biomarker positive expression defined by IHC as CPS ≥ 1 , had confirmed CR or PR per RECIST 1.1 by investigator, and received ≥ 1 dose of study drug.

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

End point timeframe:

Up to ~43 months (through database cut-off date of 18-September-2019)

| End point values | Cohort A Participants with PD-L1 CPS ≥1 | Cohort B Participants with PD-L1 CPS ≥1 | | |
|-------------------------------|--|--|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 7 | 6 | | |
| Units: Months | | | | |
| median (full range (min-max)) | 9.8 (4.0 to 35.4) | 7.5 (4.2 to 32.9) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: DCR per RECIST 1.1 by Investigator in all Cohort A and Cohort B Participants

| | |
|-----------------|--|
| End point title | DCR per RECIST 1.1 by Investigator in all Cohort A and Cohort B Participants |
|-----------------|--|

End point description:

DCR was defined as the percentage of participants in the analysis population who had a CR (Disappearance of all target lesions) or PR (≥30% decrease in SOD of target lesions) or SD (Neither sufficient shrinkage for PR nor sufficient increase for PD [at ≥20% increase in target lesion SOD and absolute SOD increase of ≥5 mm. Appearance of ≥1 new lesion is also PD]) or NN (does not qualify for CR or PD) for ≥24 weeks per RECIST 1.1 by investigator assessment. DCR was analyzed by test of binomial parameter and reported as the percentage of participants who experienced CR, PR, SD or NN per RECIST 1.1 by investigator. The analysis population included all participants in Cohort A and Cohort B who received ≥1 dose of study drug.

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

End point timeframe:

Up to ~43 months (through database cut-off date of 18-September-2019)

| End point values | Cohort A: Pembrolizumab | Cohort B: Pembrolizumab | | |
|-----------------------------------|----------------------------|----------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 285 | 91 | | |
| Units: Percentage of Participants | | | | |
| number (confidence interval 95%) | 24.9 (20.0 to 30.4) | 17.6 (10.4 to 27.0) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: DCR per RECIST 1.1 by Investigator in Subgroup of Cohort A and Cohort

B Participants with PD-L1 CPS ≥10

| | |
|-----------------|---|
| End point title | DCR per RECIST 1.1 by Investigator in Subgroup of Cohort A and Cohort B Participants with PD-L1 CPS ≥10 |
|-----------------|---|

End point description:

DCR was defined as the percentage of participants in the analysis population who had a CR (Disappearance of all target lesions) or PR (≥30% decrease in SOD of target lesions) or SD (Neither sufficient shrinkage for PR nor sufficient increase for PD [at ≥20% increase in target lesion SOD and absolute SOD increase of ≥5 mm. Appearance of ≥1 new lesion is also PD]) or NN (does not qualify for CR or PD) for ≥24 weeks per RECIST 1.1 by investigator assessment. DCR was analyzed by test of binomial parameter and reported as the percentage of participants who experienced CR, PR, SD or NN per RECIST 1.1 by investigator. The analysis population included a subgroup of participants in Cohort A and Cohort B who had a PD-L1 biomarker positive expression defined by IHC as CPS ≥10 and received ≥1 dose of study drug.

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

End point timeframe:

Up to ~43 months (through database cut-off date of 18-September-2019)

| End point values | Cohort A Participants with PD-L1 CPS ≥10 | Cohort B Participants with PD-L1 CPS ≥10 | | |
|-----------------------------------|---|---|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 43 | 22 | | |
| Units: Percentage of Participants | | | | |
| number (confidence interval 95%) | 25.6 (13.5 to 41.2) | 27.3 (10.7 to 50.2) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: DCR per RECIST 1.1 by Investigator in Subgroup of Cohort A and Cohort B Participants with PD-L1 CPS ≥1

| | |
|-----------------|--|
| End point title | DCR per RECIST 1.1 by Investigator in Subgroup of Cohort A and Cohort B Participants with PD-L1 CPS ≥1 |
|-----------------|--|

End point description:

DCR was defined as the percentage of participants in the analysis population who had a CR (Disappearance of all target lesions) or PR (≥30% decrease in SOD of target lesions) or SD (Neither sufficient shrinkage for PR nor sufficient increase for PD [at ≥20% increase in target lesion SOD and absolute SOD increase of ≥5 mm. Appearance of ≥1 new lesion is also PD]) or NN (does not qualify for CR or PD) for ≥24 weeks per RECIST 1.1 by investigator assessment. DCR was analyzed by test of binomial parameter and reported as the percentage of participants who experienced CR, PR, SD or NN per RECIST 1.1 by investigator. The analysis population included a subgroup of participants in Cohort A and Cohort B who had a PD-L1 biomarker positive expression defined by IHC as CPS ≥1 and received ≥1 dose of study drug.

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

End point timeframe:

Up to ~43 months (through database cut-off date of 18-September-2019)

| End point values | Cohort A Participants with PD-L1 CPS ≥1 | Cohort B Participants with PD-L1 CPS ≥1 | | |
|-----------------------------------|--|--|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 101 | 49 | | |
| Units: Percentage of participants | | | | |
| number (confidence interval 95%) | 24.8 (16.7 to 34.3) | 20.4 (10.2 to 34.3) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: PFS per RECIST 1.1 by Investigator in all Cohort A and Cohort B Participants

| | |
|-----------------|--|
| End point title | PFS per RECIST 1.1 by Investigator in all Cohort A and Cohort B Participants |
|-----------------|--|

End point description:

PFS was defined as the time from first dose of study treatment to the first documented PD per RECIST 1.1 by investigator assessment, or death due to any cause, whichever occurred first. Per RECIST 1.1 PD was defined as ≥20% increase in SOD of target lesions and an absolute SOD increase of ≥5 mm. The appearance of ≥1 new lesion is also PD. PFS was analyzed by KM method and reported as Median PFS per RECIST 1.1 by investigator with a 95% CI. The analysis population included all participants in Cohort A and Cohort B who received ≥1 dose of study drug.

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

End point timeframe:

Up to ~43 months (through database cut-off date of 18-September-2019)

| End point values | Cohort A: Pembrolizumab | Cohort B: Pembrolizumab | | |
|----------------------------------|----------------------------|----------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 285 | 91 | | |
| Units: Months | | | | |
| median (confidence interval 95%) | 2.1 (2.1 to 2.1) | 2.1 (2.1 to 2.3) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with PFS (PFS Rate) at Month 6 per RECIST 1.1 by Investigator in all Cohort A and Cohort B Participants

| | |
|-----------------|--|
| End point title | Percentage of Participants with PFS (PFS Rate) at Month 6 per RECIST 1.1 by Investigator in all Cohort A and Cohort B Participants |
|-----------------|--|

End point description:

PFS was defined as the time from first dose of study treatment to the first documented PD per RECIST 1.1 by investigator assessment, or death due to any cause, whichever occurred first. Per RECIST 1.1 PD was defined as ≥20% increase in SOD of target lesions and an absolute SOD increase of ≥5 mm. The

appearance of ≥ 1 new lesion is also PD. The percentage of participants with PFS (PFS rate) at Month 6 per RECIST 1.1 by investigator is reported. The analysis population included all participants in Cohort A and Cohort B who received ≥ 1 dose of study drug.

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Month 6 | |

| End point values | Cohort A: Pembrolizumab | Cohort B: Pembrolizumab | | |
|-----------------------------------|----------------------------|----------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 285 | 91 | | |
| Units: Percentage of Participants | | | | |
| number (confidence interval 95%) | 24.0 (19.2 to 29.1) | 17.8 (10.7 to 26.3) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with PFS (PFS Rate) at Month 12 per RECIST 1.1 by Investigator in all Cohort A and Cohort B Participants

| | |
|-----------------|---|
| End point title | Percentage of Participants with PFS (PFS Rate) at Month 12 per RECIST 1.1 by Investigator in all Cohort A and Cohort B Participants |
|-----------------|---|

End point description:

PFS was defined as the time from first dose of study treatment to the first documented PD per RECIST 1.1 by investigator assessment, or death due to any cause, whichever occurred first. Per RECIST 1.1 PD was defined as $\geq 20\%$ increase in SOD of target lesions and an absolute SOD increase of ≥ 5 mm. The appearance of ≥ 1 new lesion is also PD. The percentage of participants with PFS (PFS rate) at Month 12 per RECIST 1.1 by investigator is reported. The analysis population included all participants in Cohort A and Cohort B who received ≥ 1 dose of study drug.

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Month 12 | |

| End point values | Cohort A: Pembrolizumab | Cohort B: Pembrolizumab | | |
|-----------------------------------|----------------------------|----------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 285 | 91 | | |
| Units: Percentage of Participants | | | | |
| number (confidence interval 95%) | 7.7 (4.9 to 11.3) | 6.7 (2.7 to 13.1) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with PFS (PFS Rate) at Month 18 per RECIST 1.1 by Investigator in all Cohort A and Cohort B Participants

| | |
|-----------------|---|
| End point title | Percentage of Participants with PFS (PFS Rate) at Month 18 per RECIST 1.1 by Investigator in all Cohort A and Cohort B Participants |
|-----------------|---|

End point description:

PFS was defined as the time from first dose of study treatment to the first documented PD per RECIST 1.1 by investigator assessment, or death due to any cause, whichever occurred first. Per RECIST 1.1 PD was defined as $\geq 20\%$ increase in SOD of target lesions and an absolute SOD increase of ≥ 5 mm. The appearance of ≥ 1 new lesion is also PD. The percentage of participants with PFS (PFS rate) at Month 18 per RECIST 1.1 by investigator is reported. The analysis population included all participants in Cohort A and Cohort B who received ≥ 1 dose of study drug.

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

End point timeframe:

Month 18

| End point values | Cohort A: Pembrolizumab | Cohort B: Pembrolizumab | | |
|-----------------------------------|----------------------------|----------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 285 | 91 | | |
| Units: Percentage of Participants | | | | |
| number (confidence interval 95%) | 5.0 (2.8 to 8.3) | 4.4 (1.4 to 10.1) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: PFS per RECIST 1.1 by Investigator in Subgroup of Cohort A and Cohort B Participants with PD-L1 CPS ≥ 10

| | |
|-----------------|---|
| End point title | PFS per RECIST 1.1 by Investigator in Subgroup of Cohort A and Cohort B Participants with PD-L1 CPS ≥ 10 |
|-----------------|---|

End point description:

PFS was defined as the time from first dose of study treatment to the first documented PD per RECIST 1.1 by investigator assessment, or death due to any cause, whichever occurred first. Per RECIST 1.1 PD was defined as $\geq 20\%$ increase in SOD of target lesions and an absolute SOD increase of ≥ 5 mm. The appearance of ≥ 1 new lesion is also PD. PFS was analyzed by KM method and reported as Median PFS per RECIST 1.1 by investigator with a 95% CI. The analysis population included a subgroup of participants in Cohort A and Cohort B who had a PD-L1 biomarker positive expression defined by IHC as CPS ≥ 10 and received ≥ 1 dose of study drug.

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

End point timeframe:

Up to ~43 months (through database cut-off date of 18-September-2019)

| End point values | Cohort A Participants with PD-L1 CPS ≥10 | Cohort B Participants with PD-L1 CPS ≥10 | | |
|----------------------------------|---|---|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 43 | 22 | | |
| Units: Months | | | | |
| median (confidence interval 95%) | 2.1 (2.1 to 4.1) | 2.2 (2.0 to 4.8) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with PFS (PFS Rate) at Month 6 per RECIST 1.1 by Investigator in Subgroup of Cohort A and Cohort B Participants with PD-L1 CPS ≥10

| | |
|---|---|
| End point title | Percentage of Participants with PFS (PFS Rate) at Month 6 per RECIST 1.1 by Investigator in Subgroup of Cohort A and Cohort B Participants with PD-L1 CPS ≥10 |
| End point description: PFS was defined as the time from first dose of study treatment to the first documented PD per RECIST 1.1 by investigator assessment, or death due to any cause, whichever occurred first. Per RECIST 1.1 PD was defined as ≥20% increase in SOD of target lesions and an absolute SOD increase of ≥5 mm. The appearance of ≥1 new lesion is also PD. The percentage of participants with PFS (PFS rate) at Month 6 per RECIST 1.1 by investigator is reported. The analysis population included a subgroup of participants in Cohort A and Cohort B who had a PD-L1 biomarker positive expression defined by IHC as CPS ≥10 and received ≥1 dose of study drug. | |
| End point type | Secondary |
| End point timeframe: Month 6 | |

| End point values | Cohort A Participants with PD-L1 CPS ≥10 | Cohort B Participants with PD-L1 CPS ≥10 | | |
|-----------------------------------|---|---|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 43 | 22 | | |
| Units: Percentage of Participants | | | | |
| number (confidence interval 95%) | 24.2 (12.5 to 38.1) | 27.3 (11.1 to 46.4) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with PFS (PFS Rate) at Month 12 per RECIST 1.1 by Investigator in Subgroup of Cohort A and Cohort B Participants with PD-L1 CPS ≥10

| | |
|-----------------|--|
| End point title | Percentage of Participants with PFS (PFS Rate) at Month 12 per |
|-----------------|--|

End point description:

PFS was defined as the time from first dose of study treatment to the first documented PD per RECIST 1.1 by investigator assessment, or death due to any cause, whichever occurred first. Per RECIST 1.1 PD was defined as $\geq 20\%$ increase in SOD of target lesions and an absolute SOD increase of ≥ 5 mm. The appearance of ≥ 1 new lesion is also PD. The percentage of participants with PFS (PFS rate) at Month 12 per RECIST 1.1 by investigator is reported. The analysis population included a subgroup of participants in Cohort A and Cohort B who had a PD-L1 biomarker positive expression defined by IHC as CPS ≥ 10 and received ≥ 1 dose of study drug.

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

End point timeframe:

Month 12

| End point values | Cohort A Participants with PD-L1 CPS ≥ 10 | Cohort B Participants with PD-L1 CPS ≥ 10 | | |
|-----------------------------------|---|---|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 43 | 22 | | |
| Units: Percentage of Participants | | | | |
| number (confidence interval 95%) | 10.8 (3.5 to 22.8) | 13.6 (3.4 to 30.9) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with PFS (PFS Rate) at Month 18 per RECIST 1.1 by Investigator in Subgroup of Cohort A and Cohort B Participants with PD-L1 CPS ≥ 10

| | |
|-----------------|--|
| End point title | Percentage of Participants with PFS (PFS Rate) at Month 18 per RECIST 1.1 by Investigator in Subgroup of Cohort A and Cohort B Participants with PD-L1 CPS ≥ 10 |
|-----------------|--|

End point description:

PFS was defined as the time from first dose of study treatment to the first documented PD per RECIST 1.1 by investigator assessment, or death due to any cause, whichever occurred first. Per RECIST 1.1 PD was defined as $\geq 20\%$ increase in SOD of target lesions and an absolute SOD increase of ≥ 5 mm. The appearance of ≥ 1 new lesion is also PD. The percentage of participants with PFS (PFS rate) at Month 18 per RECIST 1.1 by investigator is reported. The analysis population included a subgroup of participants in Cohort A and Cohort B who had a PD-L1 biomarker positive expression defined by IHC as CPS ≥ 10 and received ≥ 1 dose of study drug.

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

End point timeframe:

Month 18

| End point values | Cohort A Participants with PD-L1 CPS ≥10 | Cohort B Participants with PD-L1 CPS ≥10 | | |
|-----------------------------------|---|---|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 43 | 22 | | |
| Units: Percentage of Participants | | | | |
| number (confidence interval 95%) | 5.4 (1.0 to 15.8) | 9.1 (1.6 to 25.1) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: PFS per RECIST 1.1 by Investigator in Subgroup of Cohort A and Cohort B Participants with PD-L1 CPS ≥1

| | |
|-----------------|--|
| End point title | PFS per RECIST 1.1 by Investigator in Subgroup of Cohort A and Cohort B Participants with PD-L1 CPS ≥1 |
|-----------------|--|

End point description:

PFS was defined as the time from first dose of study treatment to the first documented PD per RECIST 1.1 by investigator assessment, or death due to any cause, whichever occurred first. Per RECIST 1.1 PD was defined as ≥20% increase in SOD of target lesions and an absolute SOD increase of ≥5 mm. The appearance of ≥1 new lesion is also PD. PFS was analyzed by KM method and reported as Median PFS per RECIST 1.1 by investigator with a 95% CI. The analysis population included a subgroup of participants in Cohort A and Cohort B who had a PD-L1 biomarker positive expression defined by IHC as CPS ≥1 and received ≥1 dose of study drug.

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

End point timeframe:

Up to ~43 months (through database cut-off date of 18-September-2019)

| End point values | Cohort A Participants with PD-L1 CPS ≥1 | Cohort B Participants with PD-L1 CPS ≥1 | | |
|----------------------------------|--|--|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 101 | 49 | | |
| Units: Months | | | | |
| median (confidence interval 95%) | 2.1 (2.1 to 2.2) | 2.1 (2.1 to 2.2) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with PFS (PFS Rate) at Month 6 per RECIST 1.1 by Investigator in Subgroup of Cohort A and Cohort B Participants with PD-L1 CPS ≥1

| | |
|-----------------|--|
| End point title | Percentage of Participants with PFS (PFS Rate) at Month 6 per RECIST 1.1 by Investigator in Subgroup of Cohort A and Cohort B Participants with PD-L1 CPS ≥1 |
|-----------------|--|

End point description:

PFS was defined as the time from first dose of study treatment to the first documented PD per RECIST 1.1 by investigator assessment, or death due to any cause, whichever occurred first. Per RECIST 1.1 PD was defined as $\geq 20\%$ increase in SOD of target lesions and an absolute SOD increase of ≥ 5 mm. The appearance of ≥ 1 new lesion is also PD. The percentage of participants with PFS (PFS Rate) at Month 6 per RECIST 1.1 by investigator is reported. The analysis population included a subgroup of participants in Cohort A and Cohort B who had a PD-L1 biomarker positive expression defined by IHC as CPS ≥ 1 and received ≥ 1 dose of study drug.

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

End point timeframe:

Month 6

| End point values | Cohort A Participants with PD-L1 CPS ≥ 1 | Cohort B Participants with PD-L1 CPS ≥ 1 | | |
|-----------------------------------|--|--|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 101 | 49 | | |
| Units: Percentage of Participants | | | | |
| number (confidence interval 95%) | 24.1 (16.2 to 32.9) | 20.4 (10.5 to 32.6) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with PFS (PFS Rate) at Month 12 per RECIST 1.1 by Investigator in Subgroup of Cohort A and Cohort B Participants with PD-L1 CPS ≥ 1

| | |
|-----------------|---|
| End point title | Percentage of Participants with PFS (PFS Rate) at Month 12 per RECIST 1.1 by Investigator in Subgroup of Cohort A and Cohort B Participants with PD-L1 CPS ≥ 1 |
|-----------------|---|

End point description:

PFS was defined as the time from first dose of study treatment to the first documented PD per RECIST 1.1 by investigator assessment, or death due to any cause, whichever occurred first. Per RECIST 1.1 PD was defined as $\geq 20\%$ increase in SOD of target lesions and an absolute SOD increase of ≥ 5 mm. The appearance of ≥ 1 new lesion is also PD. The percentage of participants with PFS (PFS Rate) at Month 12 per RECIST 1.1 by investigator is reported. The analysis population included a subgroup of participants in Cohort A and Cohort B who had a PD-L1 biomarker positive expression defined by IHC as CPS ≥ 1 and received ≥ 1 dose of study drug.

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

End point timeframe:

Month 12

| End point values | Cohort A Participants with PD-L1 CPS ≥1 | Cohort B Participants with PD-L1 CPS ≥1 | | |
|-----------------------------------|--|--|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 101 | 49 | | |
| Units: Percentage of Participants | | | | |
| number (confidence interval 95%) | 11.0 (5.7 to 18.2) | 10.2 (3.7 to 20.5) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with PFS (PFS Rate) at Month 18 per RECIST 1.1 by Investigator in Subgroup of Cohort A and Cohort B Participants with PD-L1 CPS ≥1

| | |
|---|---|
| End point title | Percentage of Participants with PFS (PFS Rate) at Month 18 per RECIST 1.1 by Investigator in Subgroup of Cohort A and Cohort B Participants with PD-L1 CPS ≥1 |
| End point description: | |
| PFS was defined as the time from first dose of study treatment to the first documented PD per RECIST 1.1 by investigator assessment, or death due to any cause, whichever occurred first. Per RECIST 1.1 PD was defined as ≥20% increase in SOD of target lesions and an absolute SOD increase of ≥5 mm. The appearance of ≥1 new lesion is also PD. The percentage of participants with PFS (PFS Rate) at Month 18 per RECIST 1.1 by investigator is reported. The analysis population included a subgroup of participants in Cohort A and Cohort B who had a PD-L1 biomarker positive expression defined by IHC as CPS ≥1 and received ≥1 dose of study drug. | |
| End point type | Secondary |
| End point timeframe: | |
| Month 18 | |

| End point values | Cohort A Participants with PD-L1 CPS ≥1 | Cohort B Participants with PD-L1 CPS ≥1 | | |
|-----------------------------------|--|--|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 101 | 49 | | |
| Units: Percentage of Participants | | | | |
| number (confidence interval 95%) | 5.6 (1.9 to 12.3) | 6.1 (1.6 to 15.2) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: ORR per RECIST 1.1 by BICR in Subgroup of Cohort A Participants with Platinum-Free Interval (PFI)/Treatment-Free Interval (TFI) ≥3-6 Months

| | |
|-----------------|--|
| End point title | ORR per RECIST 1.1 by BICR in Subgroup of Cohort A |
|-----------------|--|

End point description:

ORR was defined as the percentage of participants in the analysis population who had a CR (Disappearance of all target lesions) or a PR (≥30% decrease in SOD of target lesions) using RECIST 1.1 based on BICR. ORR was analyzed by test of binomial parameter and reported as the percentage of participants who experienced CR or PR per RECIST 1.1 by BICR. The analysis population included a subgroup of participants in Cohort A who had a PFI/TFI (duration from end of treatment to disease recurrence) ≥3-6 months and received ≥1 dose of study drug. Per protocol PFI/TFI ≥3-6 months subgroup analysis of ORR per RECIST 1.1 by BICR was not planned or executed in Cohort B.

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

End point timeframe:

Up to ~43 months (through database cut-off date of 18-September-2019)

| End point values | Cohort A Participants with PFI/TFI ≥3-6 Months | | | |
|-----------------------------------|---|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 127 | | | |
| Units: Percentage of participants | | | | |
| number (confidence interval 95%) | 7.9 (3.8 to 14.0) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: ORR per RECIST 1.1 by BICR in Subgroup of Cohort A Participants with PFI/ TFI >6-12 Months

| | |
|-----------------|--|
| End point title | ORR per RECIST 1.1 by BICR in Subgroup of Cohort A Participants with PFI/ TFI >6-12 Months |
|-----------------|--|

End point description:

ORR was defined as the percentage of participants in the analysis population who had a CR (Disappearance of all target lesions) or a PR (≥30% decrease in SOD of target lesions) using RECIST 1.1 based on BICR. ORR was analyzed by test of binomial parameter and reported as the percentage of participants who experienced CR or PR per RECIST 1.1 by BICR. The analysis population included a subgroup of participants in Cohort A who had a PFI/TFI (duration from end of treatment to disease recurrence) >6-12 months and received ≥1 dose of study drug. Per protocol PFI/TFI >6-12 months subgroup analysis of ORR per RECIST 1.1 by BICR was not planned or executed in Cohort B.

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

End point timeframe:

Up to ~43 months (through database cut-off date of 18-September-2019)

| | | | | |
|-----------------------------------|--|--|--|--|
| End point values | Cohort A Participants with PFI/TFI >6-12 Months | | | |
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 115 | | | |
| Units: Percentage of Participants | | | | |
| number (confidence interval 95%) | 8.7 (4.2 to 15.4) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: DOR per RECIST 1.1 by BICR in Subgroup of Cohort A Participants with PFI/TFI ≥3-6 Months

| | |
|---|---|
| End point title | DOR per RECIST 1.1 by BICR in Subgroup of Cohort A Participants with PFI/TFI ≥3-6 Months |
| End point description: For participants who demonstrated a confirmed CR (disappearance of all target lesions) or PR (≥30% decrease in SOD of target lesions) per RECIST 1.1 based on BICR, DOR was defined as time from first documented CR or PR until PD or death, whichever occurs first. DOR for participants who didn't progress or die at time of analysis was censored at last tumor assessment. Per RECIST 1.1 PD is a ≥20% increase in target lesion SOD and absolute SOD increase of ≥5 mm. Appearance of ≥1 new lesion is also PD. DOR was analyzed by KM method and reported as Median DOR with a full range. The analysis population included a subgroup of participants in Cohort A who had a PFI/TFI (duration from end of treatment to disease recurrence) ≥3-6 months, had a confirmed CR or PR per RECIST 1.1 by BICR, and received ≥1 dose of study drug. Per protocol PFI/TFI ≥3-6 months subgroup analysis of DOR per RECIST 1.1 by BICR was not planned or executed in Cohort B. | |
| End point type | Secondary |
| End point timeframe: Up to ~43 months (through database cut-off date of 18-September-2019) | |

| | | | | |
|-------------------------------|---|--|--|--|
| End point values | Cohort A Participants with PFI/TFI ≥3-6 Months | | | |
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 10 | | | |
| Units: Months | | | | |
| median (full range (min-max)) | 8.3 (4.1 to 14.5) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: DOR per RECIST 1.1 by BICR in Subgroup of Cohort A Participants with PFI/TFI >6-12 Months

| | |
|---|---|
| End point title | DOR per RECIST 1.1 by BICR in Subgroup of Cohort A Participants with PFI/TFI >6-12 Months |
| End point description: | |
| For participants who demonstrated confirmed CR (disappearance of all target lesions) or PR (≥30% decrease in SOD of target lesions) per RECIST 1.1 based on BICR, DOR was defined as time from first documented CR or PR until PD or death, whichever occurs first. DOR for participants who didn't progress or die at time of analysis was censored at last tumor assessment. Per RECIST 1.1 PD is a ≥20% increase in target lesion SOD and absolute SOD increase of ≥5 mm. Appearance of ≥1 new lesion is also PD. DOR was analyzed by KM method and reported as a Median DOR with a full range. Per protocol PFI/TFI >6-12 months subgroup analysis of DOR per RECIST 1.1 by BICR was not planned or executed in Cohort B. The analysis population included a subgroup of participants in Cohort A who had a PFI/TFI (duration from end of treatment to disease recurrence) >6-12 months, had a confirmed CR or PR per RECIST 1.1 by BICR, and received ≥1 dose of study drug. | |
| End point type | Secondary |
| End point timeframe: | |
| Up to ~43 months (through database cut-off date of 18-September-2019) | |

| | | | | |
|-------------------------------|---|--|--|--|
| End point values | Cohort A Participants with PFI/TFI >6-12 Months | | | |
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 10 | | | |
| Units: Months | | | | |
| median (full range (min-max)) | 4.7 (3.9 to 34.6) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: DCR per RECIST 1.1 by BICR in Subgroup of Cohort A Participants with PFI/TFI ≥3-6 Months

| | |
|---|--|
| End point title | DCR per RECIST 1.1 by BICR in Subgroup of Cohort A Participants with PFI/TFI ≥3-6 Months |
| End point description: | |
| DCR was defined as the percentage of participants in the analysis population who have a CR (Disappearance of all target lesions) or PR (≥30% decrease in SOD of target lesions) or SD (Neither sufficient shrinkage for PR nor sufficient increase for PD [at ≥20% increase in target lesion SOD and absolute SOD increase of ≥5 mm. Appearance of ≥1 new lesion is also PD]) or NN (does not qualify for CR or PD) for ≥24 weeks per RECIST 1.1 based on BICR. DCR was analyzed by test of binomial parameter and reported as the percentage of participants who experienced CR, PR, SD or NN per RECIST 1.1 by BICR. The analysis population included a subgroup of participants in Cohort A who had a PFI/TFI (duration from end of treatment to disease recurrence) ≥3-6 months and received ≥1 dose of study drug. Per protocol PFI/TFI ≥3-6 months subgroup analysis of DCR per RECIST 1.1 by BICR was not planned or executed in Cohort B. | |
| End point type | Secondary |
| End point timeframe: | |
| Up to ~43 months (through database cut-off date of 18-September-2019) | |

| | | | | |
|-----------------------------------|---|--|--|--|
| End point values | Cohort A Participants with PFI/TFI ≥3-6 Months | | | |
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 127 | | | |
| Units: Percentage of participants | | | | |
| number (confidence interval 95%) | 18.9 (12.5 to 26.8) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: DCR per RECIST 1.1 by BICR in Subgroup of Cohort A Participants with PFI/TFI >6-12 Months

| | |
|--|--|
| End point title | DCR per RECIST 1.1 by BICR in Subgroup of Cohort A Participants with PFI/TFI >6-12 Months |
| End point description: | |
| DCR was defined as the percentage of participants in the analysis population who have a CR (Disappearance of all target lesions) or PR (≥30% decrease in SOD of target lesions) or SD (Neither sufficient shrinkage to for PR nor sufficient increase for PD [at ≥20% increase in target lesion SOD and absolute SOD increase of ≥5 mm. Appearance of ≥1 new lesion is also PD]) or NN (does not qualify for CR or PD) for ≥24 weeks per RECIST 1.1 based on BICR. DCR was analyzed by test of binomial parameter and reported as the percentage of participants who experienced CR, PR, SD or NN per RECIST 1.1 by BICR. The analysis population included a subgroup of participants in Cohort A who had a PFI/TFI (duration from end of treatment to disease recurrence) >6-12 months and received ≥1 dose of study drug. Per protocol PFI/TFI >6-12 months subgroup analysis of DCR per RECIST 1.1 by BICR was not planned or executed in Cohort B. | |
| End point type | Secondary |
| End point timeframe: | |
| Up to ~43 months (through database cut-off date of 18-September-2019) | |

| | | | | |
|-----------------------------------|--|--|--|--|
| End point values | Cohort A Participants with PFI/TFI >6-12 Months | | | |
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 115 | | | |
| Units: Percentage of Participants | | | | |
| number (confidence interval 95%) | 21.7 (14.6 to 30.4) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: PFS per RECIST 1.1 by BICR in Subgroup of Cohort A Participants with PFI/TFI ≥3-6 Months

| | |
|---|--|
| End point title | PFS per RECIST 1.1 by BICR in Subgroup of Cohort A Participants with PFI/TFI ≥3-6 Months |
| End point description: | |
| PFS was defined as the time from first dose of study treatment to the first documented PD per RECIST 1.1 based on BICR, or death due to any cause, whichever occurred first. Per RECIST 1.1 PD was defined as ≥20% increase in SOD of target lesions and an absolute SOD increase of ≥5 mm. The appearance of ≥1 new lesion is also PD. PFS was analyzed by KM method and reported as a Median PFS per RECIST 1.1 by BICR with a 95% CI. The analysis population included a subgroup of participants in Cohort A who had a PFI/TFI (duration from end of treatment to disease recurrence) ≥3-6 months and received ≥1 dose of study drug. Per protocol PFI/TFI ≥3-6 months subgroup analysis of PFS per RECIST 1.1 by BICR was not planned or executed in Cohort B. | |
| End point type | Secondary |
| End point timeframe: | |
| Up to ~43 months (through database cut-off date of 18-September-2019) | |

| | | | | |
|----------------------------------|--|--|--|--|
| End point values | Cohort A Participants with PFI/TFI ≥3-6 Months | | | |
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 127 | | | |
| Units: Months | | | | |
| median (confidence interval 95%) | 2.1 (2.1 to 2.1) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with PFS (PFS Rate) at Month 6 per RECIST 1.1 by BICR in Subgroup of Cohort A Participants with PFI/TFI ≥3-6 Months

| | |
|--|--|
| End point title | Percentage of Participants with PFS (PFS Rate) at Month 6 per RECIST 1.1 by BICR in Subgroup of Cohort A Participants with PFI/TFI ≥3-6 Months |
| End point description: | |
| PFS was defined as the time from first dose of study treatment to the first documented PD per RECIST 1.1 based on BICR, or death due to any cause, whichever occurred first. Per RECIST 1.1 PD was defined as ≥20% increase in SOD of target lesions and an absolute SOD increase of ≥5 mm. The appearance of ≥1 new lesion is also PD. The percentage of participants with PFS (PFS rate) at Month 6 per RECIST 1.1 by BICR is reported. The analysis population included a subgroup of participants in Cohort A who had a PFI/TFI (duration from end of treatment to disease recurrence) ≥3-6 months and received ≥1 dose of study drug. Per protocol PFI/TFI ≥3-6 months subgroup analysis of PFS rate at Month 6 per RECIST 1.1 by BICR was not planned or executed in Cohort B. | |
| End point type | Secondary |
| End point timeframe: | |
| Month 6 | |

| | | | | |
|-----------------------------------|---|--|--|--|
| End point values | Cohort A Participants with PFI/TFI ≥3-6 Months | | | |
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 127 | | | |
| Units: Percentage of Participants | | | | |
| number (confidence interval 95%) | 18.2 (11.9 to 25.5) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with PFS (PFS Rate) at Month 12 per RECIST 1.1 by BICR in Subgroup of Cohort A Participants with PFI/TFI ≥3-6 Months

| | |
|--|---|
| End point title | Percentage of Participants with PFS (PFS Rate) at Month 12 per RECIST 1.1 by BICR in Subgroup of Cohort A Participants with PFI/TFI ≥3-6 Months |
| End point description: | |
| PFS was defined as the time from first dose of study treatment to the first documented PD per RECIST 1.1 based on BICR, or death due to any cause, whichever occurred first. Per RECIST 1.1 PD was defined as ≥20% increase in SOD of target lesions and an absolute SOD increase of ≥5 mm. The appearance of ≥1 new lesion is also PD. The percentage of participants with PFS (PFS rate) at Month 12 per RECIST 1.1 by BICR is reported. The analysis population included a subgroup of participants in Cohort A who had a PFI/TFI (duration from end of treatment to disease recurrence) ≥3-6 months and received ≥1 dose of study drug. Per protocol PFI/TFI ≥3-6 months subgroup analysis of PFS rate at Month 12 per RECIST 1.1 by BICR was not planned or executed in Cohort B. | |
| End point type | Secondary |
| End point timeframe: | |
| Month 12 | |

| | | | | |
|-----------------------------------|---|--|--|--|
| End point values | Cohort A Participants with PFI/TFI ≥3-6 Months | | | |
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 127 | | | |
| Units: Percentage of Participants | | | | |
| number (confidence interval 95%) | 6.4 (2.8 to 11.9) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with PFS (PFS Rate) at Month 18 per RECIST 1.1 by BICR in Subgroup of Cohort A Participants with PFI/TFI ≥3-6 Months

| | |
|-----------------|--|
| End point title | Percentage of Participants with PFS (PFS Rate) at Month 18 per |
|-----------------|--|

End point description:

PFS was defined as the time from first dose of study treatment to the first documented PD per RECIST 1.1 based on BICR, or death due to any cause, whichever occurred first. Per RECIST 1.1 PD was defined as ≥20% increase in SOD of target lesions and an absolute SOD increase of ≥5 mm. The appearance of ≥1 new lesion is also PD. The percentage of participants with PFS (PFS rate) at Month 18 per RECIST 1.1 by BICR is reported. The analysis population included a subgroup of participants in Cohort A who had a PFI/TFI (duration from end of treatment to disease recurrence) ≥3-6 months and received ≥1 dose of study drug. Per protocol PFI/TFI ≥3-6 months subgroup analysis of PFS rate at Month 18 per RECIST 1.1 by BICR was not planned or executed in Cohort B.

End point type Secondary

End point timeframe:

Month 18

| End point values | Cohort A Participants with PFI/TFI ≥3-6 Months | | | |
|-----------------------------------|--|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 127 | | | |
| Units: Percentage of Participants | | | | |
| number (confidence interval 95%) | 1.1 (0.1 to 5.2) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: PFS per RECIST 1.1 by BICR in Subgroup of Cohort A Participants with PFI/TFI >6-12 Months

End point title PFS per RECIST 1.1 by BICR in Subgroup of Cohort A Participants with PFI/TFI >6-12 Months

End point description:

PFS was defined as the time from first dose of study treatment to the first documented PD per RECIST 1.1 based on BICR, or death due to any cause, whichever occurred first. Per RECIST 1.1 PD was defined as ≥20% increase in SOD of target lesions and an absolute SOD increase of ≥5 mm. The appearance of ≥1 new lesion is also PD. PFS was analyzed by KM method and reported as Median PFS per RECIST 1.1 by investigator with a 95% CI. The analysis population included a subgroup of participants in Cohort A who had a PFI/TFI (duration from end of treatment to disease recurrence) >6-12 months and received ≥1 dose of study drug. Per protocol PFI/TFI >6-12 months subgroup analysis of PFS per RECIST 1.1 by BICR was not planned or executed in Cohort B.

End point type Secondary

End point timeframe:

Up to ~43 months (through database cut-off date of 18-September-2019)

| | | | | |
|----------------------------------|--|--|--|--|
| End point values | Cohort A Participants with PFI/TFI >6-12 Months | | | |
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 115 | | | |
| Units: Months | | | | |
| median (confidence interval 95%) | 2.1 (2.1 to 2.2) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with PFS (PFS Rate) at Month 6 per RECIST 1.1 by BICR in Subgroup of Cohort A Participants with PFI/TFI >6-12 Months

| | |
|--|---|
| End point title | Percentage of Participants with PFS (PFS Rate) at Month 6 per RECIST 1.1 by BICR in Subgroup of Cohort A Participants with PFI/TFI >6-12 Months |
| End point description: | |
| PFS was defined as the time from first dose of study treatment to the first documented PD per RECIST 1.1 based on BICR, or death due to any cause, whichever occurred first. Per RECIST 1.1 PD was defined as ≥20% increase in SOD of target lesions and an absolute SOD increase of ≥5 mm. The appearance of ≥1 new lesion is also PD. The percentage of participants with PFS (PFS rate) at Month 6 per RECIST 1.1 by BICR is reported. The analysis population included a subgroup of participants in Cohort A who had a PFI/TFI (duration from end of treatment to disease recurrence) >6-12 months and received ≥1 dose of study drug. Per protocol PFI/TFI >6-12 months subgroup analysis of PFS rate at Month 6 per RECIST 1.1 by BICR was not planned or executed in Cohort B. | |
| End point type | Secondary |
| End point timeframe: | |
| Month 6 | |

| | | | | |
|-----------------------------------|--|--|--|--|
| End point values | Cohort A Participants with PFI/TFI >6-12 Months | | | |
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 115 | | | |
| Units: Percentage of Participants | | | | |
| number (confidence interval 95%) | 23.1 (15.7 to 31.4) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with PFS (PFS Rate) at Month 12 per RECIST 1.1 by BICR in Subgroup of Cohort A Participants with PFI/TFI >6-12 Months

| | | | | |
|-----------------|---|--|--|--|
| End point title | Percentage of Participants with PFS (PFS Rate) at Month 12 per RECIST 1.1 by BICR in Subgroup of Cohort A Participants with | | | |
|-----------------|---|--|--|--|

End point description:

PFS was defined as the time from first dose of study treatment to the first documented PD per RECIST 1.1 based on BICR, or death due to any cause, whichever occurred first. Per RECIST 1.1 PD was defined as $\geq 20\%$ increase in SOD of target lesions and an absolute SOD increase of ≥ 5 mm. The appearance of ≥ 1 new lesion is also PD. The percentage of participants with PFS (PFS rate) at Month 12 per RECIST 1.1 by BICR is reported. The analysis population included a subgroup of participants in Cohort A who had a PFI/TFI (duration from end of treatment to disease recurrence) >6-12 months and received ≥ 1 dose of study drug. Per protocol PFI/TFI >6-12 months subgroup analysis of PFS rate at Month 12 per RECIST 1.1 by BICR was not planned or executed in Cohort B.

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

End point timeframe:

Month 12

| End point values | Cohort A Participants with PFI/TFI >6-12 Months | | | |
|-----------------------------------|--|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 115 | | | |
| Units: Percentage of Participants | | | | |
| number (confidence interval 95%) | 12.0 (6.4 to 19.4) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with PFS (PFS Rate) at Month 18 per RECIST 1.1 by BICR in Subgroup of Cohort A Participants with PFI/TFI >6-12 Months

| | |
|-----------------|--|
| End point title | Percentage of Participants with PFS (PFS Rate) at Month 18 per RECIST 1.1 by BICR in Subgroup of Cohort A Participants with PFI/TFI >6-12 Months |
|-----------------|--|

End point description:

PFS was defined as the time from first dose of study treatment to the first documented PD per RECIST 1.1 based on BICR, or death due to any cause, whichever occurred first. Per RECIST 1.1 PD was defined as $\geq 20\%$ increase in SOD of target lesions and an absolute SOD increase of ≥ 5 mm. The appearance of ≥ 1 new lesion is also PD. The percentage of participants with PFS (PFS rate) at Month 18 per RECIST 1.1 by BICR is reported. The analysis population included a subgroup of participants in Cohort A who had a PFI/TFI (duration from end of treatment to disease recurrence) >6-12 months and received ≥ 1 dose of study drug. Per protocol PFI/TFI >6-12 months subgroup analysis of PFS rate at Month 18 per RECIST 1.1 by BICR was not planned or executed in Cohort B.

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

End point timeframe:

Month 18

| | | | | |
|-----------------------------------|--|--|--|--|
| End point values | Cohort A Participants with PFI/TFI >6-12 Months | | | |
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 115 | | | |
| Units: Percentage of Participants | | | | |
| number (confidence interval 95%) | 8.0 (3.5 to 14.9) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: ORR per RECIST 1.1 by Investigator in Subgroup of Cohort A Participants with PFI/ TFI ≥3-6 Months

| | |
|---|--|
| End point title | ORR per RECIST 1.1 by Investigator in Subgroup of Cohort A Participants with PFI/ TFI ≥3-6 Months |
| End point description: | |
| ORR was defined as the percentage of participants in the analysis population who had a CR (Disappearance of all target lesions) or a PR (≥30% decrease in SOD of target lesions) using RECIST 1.1 based on investigator assessment. ORR was analyzed by test of binomial parameter and reported as the percentage of participants who experienced CR or PR per RECIST 1.1 by investigator. The analysis population included a subgroup of participants in Cohort A who had a PFI/TFI (duration from end of treatment to disease recurrence) ≥3-6 months and received ≥1 dose of study drug. Per protocol PFI/TFI ≥3-6 months subgroup analysis of ORR per RECIST 1.1 by investigator was not planned or executed in Cohort B. | |
| End point type | Secondary |
| End point timeframe: | |
| Up to ~43 months (through database cut-off date of 18-September-2019) | |

| | | | | |
|-----------------------------------|---|--|--|--|
| End point values | Cohort A Participants with PFI/TFI ≥3-6 Months | | | |
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 127 | | | |
| Units: Percentage of participants | | | | |
| number (confidence interval 95%) | 8.7 (4.4 to 15.0) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: ORR per RECIST 1.1 by Investigator in Subgroup of Cohort A Participants with PFI/ TFI >6-12 Months

| | | | | |
|-----------------|---|--|--|--|
| End point title | ORR per RECIST 1.1 by Investigator in Subgroup of Cohort A Participants with PFI/ TFI >6-12 Months | | | |
|-----------------|---|--|--|--|

End point description:

ORR was defined as the percentage of participants in the analysis population who had a CR (Disappearance of all target lesions) or a PR ($\geq 30\%$ decrease in SOD of target lesions) using RECIST 1.1 based on investigator assessment. ORR was defined as the percentage of participants in the analysis population who had a CR (Disappearance of all target lesions) or a PR ($\geq 30\%$ decrease in SOD of target lesions) using RECIST 1.1 based on investigator assessment. ORR was analyzed by test of binomial parameter and reported as the percentage of participants who experienced CR or PR per RECIST 1.1 by investigator. The analysis population included a subgroup of participants in Cohort A who had a PFI/TFI (duration from end of treatment to disease recurrence) >6 -12 months and received ≥ 1 dose of study drug. Per protocol PFI/TFI >6 -12 months subgroup analysis of ORR per RECIST 1.1 by investigator was not planned or executed in Cohort B.

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

End point timeframe:

Up to ~43 months (through database cut-off date of 18-September-2019)

| | | | | |
|-----------------------------------|--|--|--|--|
| End point values | Cohort A Participants with PFI/TFI >6-12 Months | | | |
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 115 | | | |
| Units: Percentage of Participants | | | | |
| number (confidence interval 95%) | 5.2 (1.9 to 11.0) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: DOR per RECIST 1.1 by Investigator in Subgroup of Cohort A Participants with PFI/TFI ≥ 3 -6 Months

| | |
|-----------------|---|
| End point title | DOR per RECIST 1.1 by Investigator in Subgroup of Cohort A Participants with PFI/TFI ≥ 3 -6 Months |
|-----------------|---|

End point description:

For participants who demonstrated a confirmed CR (disappearance of all target lesions) or PR ($\geq 30\%$ decrease in SOD of target lesions) per RECIST 1.1 by investigator assessment, DOR was defined as time from first documented CR or PR until PD or death, whichever occurs first. DOR for participants who didn't progress or die at time of analysis was censored at last tumor assessment. Per RECIST 1.1 PD is $\geq 20\%$ increase in target lesion SOD and absolute SOD increase of ≥ 5 mm. Appearance of ≥ 1 new lesion is also PD. DOR was analyzed by KM method and reported as Median DOR with a full range. The analysis population included a subgroup of participants in Cohort A who had a PFI/TFI (duration from end of treatment to disease recurrence) ≥ 3 -6 months, had a confirmed CR or PR per RECIST 1.1 by BICR, and received ≥ 1 dose of study drug. Per protocol PFI/TFI ≥ 3 -6 months subgroup analysis of DOR per RECIST 1.1 by investigator was not planned or executed in Cohort B.

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

End point timeframe:

Up to ~43 months (through database cut-off date of 18-September-2019)

| End point values | Cohort A Participants with PFI/TFI ≥3-6 Months | | | |
|-------------------------------|---|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 11 | | | |
| Units: Months | | | | |
| median (full range (min-max)) | 8.4 (5.0 to 17.2) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: DOR per RECIST 1.1 by Investigator in Subgroup of Cohort A Participants with PFI/TFI >6-12 Months

| | |
|-----------------|--|
| End point title | DOR per RECIST 1.1 by Investigator in Subgroup of Cohort A Participants with PFI/TFI >6-12 Months |
|-----------------|--|

End point description:

For participants who demonstrated confirmed CR (disappearance of all target lesions) or PR (≥30% decrease in SOD of target lesions) per RECIST 1.1 by investigator assessment, DOR was defined as time from first documented CR or PR until PD or death, whichever occurs first. DOR for participants who didn't progress or die at time of analysis was censored at last tumor assessment. Per RECIST 1.1 PD is ≥20% increase in target lesion SOD and absolute SOD increase of ≥5 mm. Appearance of ≥1 new lesion is also PD. DOR was analyzed by KM method and reported as Median DOR with a full range. The analysis population included a subgroup of participants in Cohort A who had a PFI/TFI (duration from end of treatment to disease recurrence) >6-12 months, had a confirmed CR or PR per RECIST 1.1 by BICR, and received ≥1 dose of study drug. Per protocol PFI/TFI >6-12 months subgroup analysis of DOR per RECIST 1.1 by investigator was not planned or executed in Cohort B.

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

End point timeframe:

Up to ~43 months (through database cut-off date of 18-September-2019)

| End point values | Cohort A Participants with PFI/TFI >6-12 Months | | | |
|-------------------------------|--|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 6 | | | |
| Units: Months | | | | |
| median (full range (min-max)) | 9.7 (4.0 to 34.6) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: DCR per RECIST 1.1 by Investigator in Subgroup of Cohort A Participants with PFI/TFI ≥3-6 Months

| | |
|---|--|
| End point title | DCR per RECIST 1.1 by Investigator in Subgroup of Cohort A Participants with PFI/TFI ≥3-6 Months |
| End point description: | |
| DCR was defined as the percentage of participants in the analysis population who have CR (Disappearance of all target lesions) or PR (≥30% decrease in SOD of target lesions) or SD (Neither sufficient shrinkage for PR nor sufficient increase for PD [at ≥20% increase in target lesion SOD and absolute SOD increase of ≥5 mm. Appearance of ≥1 new lesion is also PD]) or NN (doesn't qualify for CR or PD) for ≥24 weeks per RECIST 1.1 by investigator assessment. DCR was analyzed by test of binomial parameter and reported as the percentage of participants who experienced CR, PR, SD or NN per RECIST 1.1 by investigator. The analysis population included a subgroup of participants in Cohort A who had a PFI/TFI (duration from end of treatment to disease recurrence) ≥3-6 months and received ≥1 dose of study drug. Per protocol PFI/TFI ≥3-6 months subgroup analysis of DCR per RECIST 1.1 by investigator was not planned or executed in Cohort B. | |
| End point type | Secondary |
| End point timeframe: | |
| Up to ~43 months (through database cut-off date of 18-September-2019) | |

| | | | | |
|-----------------------------------|--|--|--|--|
| End point values | Cohort A Participants with PFI/TFI ≥3-6 Months | | | |
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 127 | | | |
| Units: Percentage of participants | | | | |
| number (confidence interval 95%) | 21.3 (14.5 to 29.4) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: DCR per RECIST 1.1 by Investigator in Subgroup of Cohort A Participants with PFI/TFI >6-12 Months

| | |
|---|---|
| End point title | DCR per RECIST 1.1 by Investigator in Subgroup of Cohort A Participants with PFI/TFI >6-12 Months |
| End point description: | |
| DCR was defined as the percentage of participants in the analysis population who have CR (Disappearance of all target lesions) or PR (≥30% decrease in SOD of target lesions) or SD (Neither sufficient shrinkage for PR nor sufficient increase for PD [at ≥20% increase in target lesion SOD and absolute SOD increase of ≥5 mm. Appearance of ≥1 new lesion is also PD]) or NN (doesn't qualify for CR or PD) for ≥24 weeks per RECIST 1.1 by investigator assessment. DCR was analyzed by test of binomial parameter and reported as the percentage of participants who experienced CR, PR, SD or NN per RECIST 1.1 by investigator. The analysis population included a subgroup of participants in Cohort A who had a PFI/TFI (duration from end of treatment to disease recurrence) >6-12 months and received ≥1 dose of study drug. Per protocol PFI/TFI >6-12 months subgroup analysis of DCR per RECIST 1.1 by investigator was not planned or executed in Cohort B. | |
| End point type | Secondary |
| End point timeframe: | |
| Up to ~43 months (through database cut-off date of 18-September-2019) | |

| | | | | |
|-----------------------------------|--|--|--|--|
| End point values | Cohort A Participants with PFI/TFI >6-12 Months | | | |
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 115 | | | |
| Units: Percentage of participants | | | | |
| number (confidence interval 95%) | 23.5 (16.1 to 32.3) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: PFS per RECIST 1.1 by Investigator in Subgroup of Cohort A Participants with PFI/TFI ≥3-6 Months

| | |
|--|--|
| End point title | PFS per RECIST 1.1 by Investigator in Subgroup of Cohort A Participants with PFI/TFI ≥3-6 Months |
| End point description: | |
| PFS was defined as the time from first dose of study treatment to the first documented PD per RECIST 1.1 by investigator assessment, or death due to any cause, whichever occurred first. Per RECIST 1.1 PD was defined as ≥20% increase in SOD of target lesions and an absolute SOD increase of ≥5 mm. The appearance of ≥1 new lesion is also PD. PFS was analyzed by KM method and reported as a Median PFS per RECIST 1.1 by investigator with a 95% CI. The analysis population included a subgroup of participants in Cohort A who had a PFI/TFI (duration from end of treatment to disease recurrence) ≥3-6 months and received ≥1 dose of study drug. Per protocol PFI/TFI ≥3-6 months subgroup analysis of PFS per RECIST 1.1 by investigator was not planned or executed in Cohort B. | |
| End point type | Secondary |
| End point timeframe: | |
| Up to ~43 months (through database cut-off date of 18-September-2019) | |

| | | | | |
|----------------------------------|---|--|--|--|
| End point values | Cohort A Participants with PFI/TFI ≥3-6 Months | | | |
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 127 | | | |
| Units: Months | | | | |
| median (confidence interval 95%) | 2.1 (2.1 to 2.1) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with PFS (PFS Rate) at Month 6 per RECIST 1.1 by Investigator in Subgroup of Cohort A Participants with PFI/TFI ≥3-6 Months

| | |
|-----------------|--|
| End point title | Percentage of Participants with PFS (PFS Rate) at Month 6 per RECIST 1.1 by Investigator in Subgroup of Cohort A Participants with PFI/TFI ≥3-6 Months |
|-----------------|--|

End point description:

PFS was defined as the time from first dose of study treatment to the first documented PD per RECIST 1.1 by investigator assessment, or death due to any cause, whichever occurred first. Per RECIST 1.1 PD was defined as $\geq 20\%$ increase in SOD of target lesions and an absolute SOD increase of ≥ 5 mm. The appearance of ≥ 1 new lesion is also PD. The percentage of participants with PFS (PFS rate) at Month 6 per RECIST 1.1 by investigator is reported. The analysis population included a subgroup of participants in Cohort A who had a PFI/TFI (duration from end of treatment to disease recurrence) ≥ 3 -6 months and received ≥ 1 dose of study drug. Per protocol PFI/TFI ≥ 3 -6 months subgroup analysis of PFS rate at Month 6 per RECIST 1.1 by investigator was not planned or executed in Cohort B.

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

End point timeframe:

Month 6

| | | | | |
|-----------------------------------|--|--|--|--|
| End point values | Cohort A Participants with PFI/TFI ≥ 3 -6 Months | | | |
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 127 | | | |
| Units: Percentage of Participants | | | | |
| number (confidence interval 95%) | 20.5 (13.9 to 27.9) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with PFS (PFS Rate) at Month 12 per RECIST 1.1 by Investigator in Subgroup of Cohort A Participants with PFI/TFI ≥ 3 -6 Months

| | |
|-----------------|--|
| End point title | Percentage of Participants with PFS (PFS Rate) at Month 12 per RECIST 1.1 by Investigator in Subgroup of Cohort A Participants with PFI/TFI ≥ 3 -6 Months |
|-----------------|--|

End point description:

PFS was defined as the time from first dose of study treatment to the first documented PD per RECIST 1.1 by investigator assessment, or death due to any cause, whichever occurred first. Per RECIST 1.1 PD was defined as $\geq 20\%$ increase in SOD of target lesions and an absolute SOD increase of ≥ 5 mm. The appearance of ≥ 1 new lesion is also PD. The percentage of participants with PFS (PFS rate) at Month 12 per RECIST 1.1 by investigator is reported. The analysis population included a subgroup of participants in Cohort A who had a PFI/TFI (duration from end of treatment to disease recurrence) ≥ 3 -6 months and received ≥ 1 dose of study drug. Per protocol PFI/TFI ≥ 3 -6 months subgroup analysis of PFS rate at Month 12 per RECIST 1.1 by investigator was not planned or executed in Cohort B.

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

End point timeframe:

Month 12

| | | | | |
|-----------------------------------|---|--|--|--|
| End point values | Cohort A Participants with PFI/TFI ≥3-6 Months | | | |
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 127 | | | |
| Units: Percentage of Participants | | | | |
| number (confidence interval 95%) | 6.8 (3.2 to 12.3) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with PFS (PFS Rate) at Month 18 per RECIST 1.1 by Investigator in Subgroup of Cohort A Participants with PFI/TFI ≥3-6 Months

| | |
|---|--|
| End point title | Percentage of Participants with PFS (PFS Rate) at Month 18 per RECIST 1.1 by Investigator in Subgroup of Cohort A Participants with PFI/TFI ≥3-6 Months |
| End point description: | |
| PFS was defined as the time from first dose of study treatment to the first documented PD per RECIST 1.1 by investigator assessment, or death due to any cause, whichever occurred first. Per RECIST 1.1 PD was defined as ≥20% increase in SOD of target lesions and an absolute SOD increase of ≥5 mm. The appearance of ≥1 new lesion is also PD. The percentage of participants with PFS (PFS rate) at Month 18 per RECIST 1.1 by investigator is reported. The analysis population included a subgroup of participants in Cohort A who had a PFI/TFI (duration from end of treatment to disease recurrence) ≥3-6 months and received ≥1 dose of study drug. Per protocol PFI/TFI ≥3-6 months subgroup analysis of PFS rate at Month 18 per RECIST 1.1 by investigator was not planned or executed in Cohort B. | |
| End point type | Secondary |
| End point timeframe: | |
| Month 18 | |

| | | | | |
|-----------------------------------|---|--|--|--|
| End point values | Cohort A Participants with PFI/TFI ≥3-6 Months | | | |
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 127 | | | |
| Units: Percentage of Participants | | | | |
| number (confidence interval 95%) | 4.0 (1.4 to 8.8) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: PFS per RECIST 1.1 by Investigator in Subgroup of Cohort A Participants with PFI/TFI >6-12 Months

| | |
|-----------------|--|
| End point title | PFS per RECIST 1.1 by Investigator in Subgroup of Cohort A Participants with PFI/TFI >6-12 Months |
|-----------------|--|

End point description:

PFS was defined as the time from first dose of study treatment to the first documented PD per RECIST 1.1 by investigator assessment, or death due to any cause, whichever occurred first. Per RECIST 1.1 PD was defined as $\geq 20\%$ increase in SOD of target lesions and an absolute SOD increase of ≥ 5 mm. The appearance of ≥ 1 new lesion is also PD. PFS was analyzed by KM method and reported as a Median PFS per RECIST 1.1 by investigator with a 95% CI. The analysis population included a subgroup of participants in Cohort A who had a PFI/TFI (duration from end of treatment to disease recurrence) > 6 -12 months and received ≥ 1 dose of study drug. Per protocol PFI/TFI > 6 -12 months subgroup analysis of PFS per RECIST 1.1 by investigator was not planned or executed in Cohort B.

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

End point timeframe:

Up to ~43 months (through database cut-off date of 18-September-2019)

| | | | | |
|----------------------------------|--|--|--|--|
| End point values | Cohort A Participants with PFI/TFI >6-12 Months | | | |
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 115 | | | |
| Units: Months | | | | |
| median (confidence interval 95%) | 2.1 (2.1 to 2.1) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with PFS (PFS Rate) at Month 6 per RECIST 1.1 by Investigator in Subgroup of Cohort A Participants with PFI/TFI > 6 -12 Months

| | |
|-----------------|---|
| End point title | Percentage of Participants with PFS (PFS Rate) at Month 6 per RECIST 1.1 by Investigator in Subgroup of Cohort A Participants with PFI/TFI > 6 -12 Months |
|-----------------|---|

End point description:

PFS was defined as the time from first dose of study treatment to the first documented PD per RECIST 1.1 by investigator assessment, or death due to any cause, whichever occurred first. Per RECIST 1.1 PD was defined as $\geq 20\%$ increase in SOD of target lesions and an absolute SOD increase of ≥ 5 mm. The appearance of ≥ 1 new lesion is also PD. The percentage of participants with PFS (PFS rate) at Month 6 per RECIST 1.1 by investigator is reported. The analysis population included a subgroup of participants in Cohort A who had a PFI/TFI (duration from end of treatment to disease recurrence) > 6 -12 months and received ≥ 1 dose of study drug. Per protocol PFI/TFI > 6 -12 months subgroup analysis of PFS rate at Month 6 per RECIST 1.1 by investigator was not planned or executed in Cohort B.

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

End point timeframe:

Month 6

| | | | | |
|-----------------------------------|--|--|--|--|
| End point values | Cohort A Participants with PFI/TFI >6-12 Months | | | |
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 115 | | | |
| Units: Percentage of Participants | | | | |
| number (confidence interval 95%) | 22.6 (15.5 to 30.6) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with PFS (PFS Rate) at Month 12 per RECIST 1.1 by Investigator in Subgroup of Cohort A Participants with PFI/TFI >6-12 Months

| | |
|-----------------|---|
| End point title | Percentage of Participants with PFS (PFS Rate) at Month 12 per RECIST 1.1 by Investigator in Subgroup of Cohort A Participants with PFI/TFI >6-12 Months |
|-----------------|---|

End point description:

PFS was defined as the time from first dose of study treatment to the first documented PD per RECIST 1.1 by investigator assessment, or death due to any cause, whichever occurred first. Per RECIST 1.1 PD was defined as $\geq 20\%$ increase in SOD of target lesions and an absolute SOD increase of ≥ 5 mm. The appearance of ≥ 1 new lesion is also PD. The percentage of participants with PFS (PFS rate) at Month 12 per RECIST 1.1 by investigator is reported. The analysis population included a subgroup of participants in Cohort A who had a PFI/TFI (duration from end of treatment to disease recurrence) >6-12 months and received ≥ 1 dose of study drug. Per protocol PFI/TFI >6-12 months subgroup analysis of PFS rate at Month 12 per RECIST 1.1 by investigator was not planned or executed in Cohort B.

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

End point timeframe:

Month 12

| | | | | |
|-----------------------------------|--|--|--|--|
| End point values | Cohort A Participants with PFI/TFI >6-12 Months | | | |
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 115 | | | |
| Units: Percentage of Participants | | | | |
| number (confidence interval 95%) | 5.6 (2.3 to 10.9) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with PFS (PFS Rate) at Month 18 per RECIST 1.1 by Investigator in Subgroup of Cohort A Participants with PFI/TFI >6-12 Months

| | |
|-----------------|--|
| End point title | Percentage of Participants with PFS (PFS Rate) at Month 18 per |
|-----------------|--|

End point description:

PFS was defined as the time from first dose of study treatment to the first documented PD per RECIST 1.1 by investigator assessment, or death due to any cause, whichever occurred first. Per RECIST 1.1 PD was defined as $\geq 20\%$ increase in SOD of target lesions and an absolute SOD increase of ≥ 5 mm. The appearance of ≥ 1 new lesion is also PD. The percentage of participants with PFS (PFS rate) at Month 18 per RECIST 1.1 by investigator is reported. The analysis population included a subgroup of participants in Cohort A who had a PFI/TFI (duration from end of treatment to disease recurrence) >6-12 months and received ≥ 1 dose of study drug. Per protocol PFI/TFI >6-12 months subgroup analysis of PFS rate at Month 18 per RECIST 1.1 by investigator was not planned or executed in Cohort B.

End point type Secondary

End point timeframe:

Month 18

| End point values | Cohort A Participants with PFI/TFI >6-12 Months | | | |
|-----------------------------------|--|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 115 | | | |
| Units: Percentage of Participants | | | | |
| number (confidence interval 95%) | 3.7 (1.2 to 8.5) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS) in all Cohort A and Cohort B Participants

End point title Overall Survival (OS) in all Cohort A and Cohort B Participants

End point description:

OS was defined as the time from the first dose of study drug to death due to any cause. OS was analyzed by KM method and reported as Median OS with a 95% CI. The analysis population was all participants in Cohort A and Cohort B that received ≥ 1 dose of study drug.

End point type Secondary

End point timeframe:

Up to ~58.8 months (through database cut-off date of 18-March-2021)

| End point values | Cohort A: Pembrolizumab | Cohort B: Pembrolizumab | | |
|----------------------------------|----------------------------|----------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 285 | 91 | | |
| Units: Months | | | | |
| median (confidence interval 95%) | 18.7 (17.0 to 22.4) | 17.6 (13.3 to 24.4) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with OS (OS Rate) at Month 6 in all Cohort A and Cohort B Participants

| | |
|-----------------|---|
| End point title | Percentage of Participants with OS (OS Rate) at Month 6 in all Cohort A and Cohort B Participants |
|-----------------|---|

End point description:

OS was defined as the time from the first dose of study drug to death due to any cause. The percentage of participants with OS (OS rate) at Month 6 is reported. The analysis population was all participants in Cohort A and Cohort B that received ≥ 1 dose of study drug.

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

End point timeframe:

Month 6

| End point values | Cohort A: Pembrolizumab | Cohort B: Pembrolizumab | | |
|-----------------------------------|----------------------------|----------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 285 | 91 | | |
| Units: Percentage of Participants | | | | |
| number (confidence interval 95%) | 82.5 (77.5 to 86.4) | 79.0 (69.0 to 86.0) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with OS (OS Rate) at Month 12 in all Cohort A and Cohort B Participants

| | |
|-----------------|--|
| End point title | Percentage of Participants with OS (OS Rate) at Month 12 in all Cohort A and Cohort B Participants |
|-----------------|--|

End point description:

OS was defined as the time from the first dose of study drug to death due to any cause. The percentage of participants with OS (OS rate) at Month 12 is reported. The analysis population was all participants in Cohort A and Cohort B that received ≥ 1 dose of study drug.

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

End point timeframe:

Month 12

| End point values | Cohort A: Pembrolizumab | Cohort B: Pembrolizumab | | |
|-----------------------------------|----------------------------|----------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 285 | 91 | | |
| Units: Percentage of Participants | | | | |
| number (confidence interval 95%) | 66.0 (60.1 to 71.1) | 66.6 (55.8 to 75.3) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with OS (OS Rate) at Month 18 in all Cohort A and Cohort B Participants

| | |
|-----------------|--|
| End point title | Percentage of Participants with OS (OS Rate) at Month 18 in all Cohort A and Cohort B Participants |
|-----------------|--|

End point description:

OS was defined as the time from the first dose of study drug to death due to any cause. The percentage of participants with OS (OS rate) at Month 18 is reported. The analysis population was all participants in Cohort A and Cohort B that received ≥ 1 dose of study drug.

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

End point timeframe:

Month 18

| End point values | Cohort A: Pembrolizumab | Cohort B: Pembrolizumab | | |
|-----------------------------------|----------------------------|----------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 285 | 91 | | |
| Units: Percentage of Participants | | | | |
| number (confidence interval 95%) | 51.3 (45.4 to 57.0) | 48.5 (37.8 to 58.4) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with OS (OS Rate) at Month 24 in all Cohort A and Cohort B Participants

| | |
|-----------------|--|
| End point title | Percentage of Participants with OS (OS Rate) at Month 24 in all Cohort A and Cohort B Participants |
|-----------------|--|

End point description:

OS was defined as the time from the first dose of study drug to death due to any cause. The percentage of participants with OS (OS rate) at Month 24 is reported. The analysis population was all participants in Cohort A and Cohort B that received ≥ 1 dose of study drug.

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

End point timeframe:

Month 24

| End point values | Cohort A: Pembrolizumab | Cohort B: Pembrolizumab | | |
|-----------------------------------|----------------------------|----------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 285 | 91 | | |
| Units: Percentage of Participants | | | | |
| number (confidence interval 95%) | 40.5 (34.7 to 46.1) | 40.6 (30.4 to 50.6) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: OS in Subgroup of Cohort A and Cohort B Participants with PD-L1 CPS ≥ 10

| | |
|-----------------|---|
| End point title | OS in Subgroup of Cohort A and Cohort B Participants with PD-L1 CPS ≥ 10 |
|-----------------|---|

End point description:

OS was defined as the time from the first dose of study drug to death due to any cause. OS was analyzed by KM method and is reported as Median OS with a 95% CI. A value of 9999 = Based on the statistical model used for data analysis, upper limit of 95% CI was not reached by the data cut-off date. The analysis population included a subgroup of participants in Cohort A and Cohort B who had a PD-L1 biomarker positive expression defined by IHC as CPS ≥ 10 and received ≥ 1 dose of study drug.

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

End point timeframe:

Up to ~43 months (through database cut-off date of 18-September-2019)

| End point values | Cohort A Participants with PD-L1 CPS ≥ 10 | Cohort B Participants with PD-L1 CPS ≥ 10 | | |
|----------------------------------|---|---|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 43 | 22 | | |
| Units: Months | | | | |
| median (confidence interval 95%) | 21.9 (12.9 to 26.8) | 24.0 (14.5 to 9999) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with OS (OS Rate) at Month 6 in Subgroup of Cohort A and Cohort B Participants with PD-L1 CPS ≥ 10

| | |
|-----------------|--|
| End point title | Percentage of Participants with OS (OS Rate) at Month 6 in Subgroup of Cohort A and Cohort B Participants with PD-L1 |
|-----------------|--|

End point description:

OS was defined as the time from the first dose of study drug to death due to any cause. The percentage of participants with OS (OS rate) at Month 6 is reported. The analysis population included a subgroup of participants in Cohort A and Cohort B who had a PD-L1 biomarker positive expression defined by IHC as CPS ≥ 10 and received ≥ 1 dose of study drug.

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

End point timeframe:

Month 6

| End point values | Cohort A Participants with PD-L1 CPS ≥ 10 | Cohort B Participants with PD-L1 CPS ≥ 10 | | |
|-----------------------------------|---|---|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 43 | 22 | | |
| Units: Percentage of Participants | | | | |
| number (confidence interval 95%) | 81.0 (65.6 to 90.0) | 95.5 (71.9 to 99.3) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with OS (OS Rate) at Month 12 in Subgroup of Cohort A and Cohort B Participants with PD-L1 CPS ≥ 10

| | |
|-----------------|---|
| End point title | Percentage of Participants with OS (OS Rate) at Month 12 in Subgroup of Cohort A and Cohort B Participants with PD-L1 CPS ≥ 10 |
|-----------------|---|

End point description:

OS was defined as the time from the first dose of study drug to death due to any cause. The percentage of participants with OS (OS rate) at Month 12 is reported. The analysis population included a subgroup of participants in Cohort A and Cohort B who had a PD-L1 biomarker positive expression defined by IHC as CPS ≥ 10 and received ≥ 1 dose of study drug.

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

End point timeframe:

Month 12

| End point values | Cohort A Participants with PD-L1 CPS ≥ 10 | Cohort B Participants with PD-L1 CPS ≥ 10 | | |
|-----------------------------------|---|---|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 43 | 22 | | |
| Units: Percentage of Participants | | | | |
| number (confidence interval 95%) | 69.1 (52.8 to 80.7) | 86.4 (63.4 to 95.4) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with OS (OS Rate) at Month 18 in Subgroup of Cohort A and Cohort B Participants with PD-L1 CPS ≥ 10

| | |
|--|---|
| End point title | Percentage of Participants with OS (OS Rate) at Month 18 in Subgroup of Cohort A and Cohort B Participants with PD-L1 CPS ≥ 10 |
| End point description: OS was defined as the time from the first dose of study drug to death due to any cause. The percentage of participants with OS (OS rate) at Month 18 is reported. The analysis population included a subgroup of participants in Cohort A and Cohort B who had a PD-L1 biomarker positive expression defined by IHC as CPS ≥ 10 and received ≥ 1 dose of study drug. | |
| End point type | Secondary |
| End point timeframe: Month 18 | |

| End point values | Cohort A Participants with PD-L1 CPS ≥ 10 | Cohort B Participants with PD-L1 CPS ≥ 10 | | |
|-----------------------------------|---|---|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 43 | 22 | | |
| Units: Percentage of Participants | | | | |
| number (confidence interval 95%) | 54.3 (38.1 to 67.9) | 59.1 (36.1 to 76.2) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: OS in Subgroup of Cohort A and Cohort B Participants with PD-L1 CPS ≥ 1

| | |
|--|--|
| End point title | OS in Subgroup of Cohort A and Cohort B Participants with PD-L1 CPS ≥ 1 |
| End point description: OS was defined as the time from the first dose of study drug to death due to any cause. OS was analyzed by KM method and is reported as Median OS with a 95% CI. The analysis population included a subgroup of participants in Cohort A and Cohort B who had a PD-L1 biomarker positive expression defined by IHC as CPS ≥ 1 and received ≥ 1 dose of study drug. | |
| End point type | Secondary |
| End point timeframe: Up to ~43 months (through database cut-off date of 18-September-2019) | |

| End point values | Cohort A Participants with PD-L1 CPS ≥1 | Cohort B Participants with PD-L1 CPS ≥1 | | |
|----------------------------------|--|--|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 101 | 49 | | |
| Units: Months | | | | |
| median (confidence interval 95%) | 20.6 (15.2 to 23.2) | 20.7 (13.6 to 27.4) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with OS (OS Rate) at Month 6 in Subgroup of Cohort A and Cohort B Participants with PD-L1 CPS ≥1

| | |
|------------------------|--|
| End point title | Percentage of Participants with OS (OS Rate) at Month 6 in Subgroup of Cohort A and Cohort B Participants with PD-L1 CPS ≥1 |
| End point description: | OS was defined as the time from the first dose of study drug to death due to any cause. The percentage of participants with OS (OS rate) at Month 6 is reported. The analysis population included a subgroup of participants in Cohort A and Cohort B who had a PD-L1 biomarker positive expression defined by IHC as CPS ≥1 and received ≥1 dose of study drug. |
| End point type | Secondary |
| End point timeframe: | |
| Month 6 | |

| End point values | Cohort A Participants with PD-L1 CPS ≥1 | Cohort B Participants with PD-L1 CPS ≥1 | | |
|-----------------------------------|--|--|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 101 | 49 | | |
| Units: Percentage of Participants | | | | |
| number (confidence interval 95%) | 80.0 (70.8 to 86.6) | 87.8 (74.8 to 94.3) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with OS (OS Rate) at Month 12 in Subgroup of Cohort A and Cohort B Participants with PD-L1 CPS ≥1

| | |
|---|--|
| End point title | Percentage of Participants with OS (OS Rate) at Month 12 in Subgroup of Cohort A and Cohort B Participants with PD-L1 CPS ≥ 1 |
| End point description: OS was defined as the time from the first dose of study drug to death due to any cause. The percentage of participants with OS (OS rate) at Month 12 is reported. The analysis population included a subgroup of participants in Cohort A and Cohort B who had a PD-L1 biomarker positive expression defined by IHC as CPS ≥ 1 and received ≥ 1 dose of study drug. | |
| End point type | Secondary |
| End point timeframe: Month 12 | |

| End point values | Cohort A Participants with PD-L1 CPS ≥ 1 | Cohort B Participants with PD-L1 CPS ≥ 1 | | |
|-----------------------------------|--|--|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 101 | 49 | | |
| Units: Percentage of Participants | | | | |
| number (confidence interval 95%) | 65.0 (54.8 to 73.5) | 75.5 (60.9 to 85.3) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with OS (OS Rate) at Month 18 in Subgroup of Cohort A and Cohort B Participants with PD-L1 CPS ≥ 1

| | |
|---|--|
| End point title | Percentage of Participants with OS (OS Rate) at Month 18 in Subgroup of Cohort A and Cohort B Participants with PD-L1 CPS ≥ 1 |
| End point description: OS was defined as the time from the first dose of study drug to death due to any cause. The percentage of participants with OS (OS rate) at Month 18 is reported. The analysis population included a subgroup of participants in Cohort A and Cohort B who had a PD-L1 biomarker positive expression defined by IHC as CPS ≥ 1 and received ≥ 1 dose of study drug. | |
| End point type | Secondary |
| End point timeframe: Month 18 | |

| End point values | Cohort A Participants with PD-L1 CPS ≥ 1 | Cohort B Participants with PD-L1 CPS ≥ 1 | | |
|-----------------------------------|--|--|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 101 | 49 | | |
| Units: Percentage of Participants | | | | |
| number (confidence interval 95%) | 52.6 (42.4 to 61.9) | 53.1 (38.3 to 65.8) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: OS in Subgroup of Cohort A Participants with PFI/TFI ≥ 3 -6 Months

| | |
|-----------------|---|
| End point title | OS in Subgroup of Cohort A Participants with PFI/TFI ≥ 3 -6 Months |
|-----------------|---|

End point description:

OS was defined as the time from the first dose of study drug to death due to any cause. OS was analyzed by KM method and is reported as Median OS with a 95% CI. The analysis population included a subgroup of participants in Cohort A who had a PFI/TFI (duration from end of treatment to disease recurrence) ≥ 3 -6 months and received ≥ 1 dose of study drug. Per protocol PFI/TFI ≥ 3 -6 months subgroup analysis of OS was not planned or executed in Cohort B.

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

End point timeframe:

Up to ~43 months (through database cut-off date of 18-September-2019)

| | | | | |
|----------------------------------|--|--|--|--|
| End point values | Cohort A Participants with PFI/TFI ≥ 3 -6 Months | | | |
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 127 | | | |
| Units: Months | | | | |
| median (confidence interval 95%) | 17.2 (14.0 to 20.6) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with OS (OS Rate) at Month 6 in Subgroup of Cohort A Participants with PFI/TFI ≥ 3 -6 Months

| | |
|-----------------|--|
| End point title | Percentage of Participants with OS (OS Rate) at Month 6 in Subgroup of Cohort A Participants with PFI/TFI ≥ 3 -6 Months |
|-----------------|--|

End point description:

OS was defined as the time from the first dose of study drug to death due to any cause. The percentage of participants with OS (OS rate) at Month 6 is reported. The analysis population included a subgroup of participants in Cohort A who had a PFI/TFI (duration from end of treatment to disease recurrence) ≥ 3 -6 months and received ≥ 1 dose of study drug. Per protocol PFI/TFI ≥ 3 -6 months subgroup analysis of OS rate at Month 6 was not planned or executed in Cohort B.

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

End point timeframe:

Month 6

| | | | | |
|-----------------------------------|---|--|--|--|
| End point values | Cohort A Participants with PFI/TFI ≥3-6 Months | | | |
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 127 | | | |
| Units: Percentage of Participants | | | | |
| number (confidence interval 95%) | 77.7 (69.4 to 84.1) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with OS (OS Rate) at Month 12 in Subgroup of Cohort A Participants with PFI/TFI ≥3-6 Months

| | |
|------------------------|---|
| End point title | Percentage of Participants with OS (OS Rate) at Month 12 in Subgroup of Cohort A Participants with PFI/TFI ≥3-6 Months |
| End point description: | OS was defined as the time from the first dose of study drug to death due to any cause. The percentage of participants with OS (OS rate) at Month 12 is reported. The analysis population included a subgroup of participants in Cohort A who had a PFI/TFI (duration from end of treatment to disease recurrence) ≥3-6 months and received ≥1 dose of study drug. Per protocol PFI/TFI >3-6 months subgroup analysis of OS rate at Month 12 was not planned or executed in Cohort B. |
| End point type | Secondary |
| End point timeframe: | |
| Month 12 | |

| | | | | |
|-----------------------------------|---|--|--|--|
| End point values | Cohort A Participants with PFI/TFI ≥3-6 Months | | | |
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 127 | | | |
| Units: Percentage of Participants | | | | |
| number (confidence interval 95%) | 62.5 (53.4 to 70.3) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with OS (OS Rate) at Month 18 in Subgroup of Cohort A Participants with PFI/TFI ≥3-6 Months

| | |
|---|--|
| End point title | Percentage of Participants with OS (OS Rate) at Month 18 in Subgroup of Cohort A Participants with PFI/TFI \geq 3-6 Months |
| End point description: | |
| OS was defined as the time from the first dose of study drug to death due to any cause. The percentage of participants with OS (OS rate) at Month 18 is reported. The analysis population included a subgroup of participants in Cohort A who had a PFI/TFI (duration from end of treatment to disease recurrence) \geq 3-6 months and received \geq 1 dose of study drug. Per protocol PFI/TFI >3-6 months subgroup analysis of OS rate at Month 18 was not planned or executed in Cohort B. | |
| End point type | Secondary |
| End point timeframe: | |
| Month 18 | |

| | | | | |
|-----------------------------------|--|--|--|--|
| End point values | Cohort A Participants with PFI/TFI \geq 3-6 Months | | | |
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 127 | | | |
| Units: Percentage of Participants | | | | |
| number (confidence interval 95%) | 45.2 (36.3 to 53.8) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: OS in Subgroup of Cohort A Participants with PFI/TFI >6-12 Months

| | |
|---|---|
| End point title | OS in Subgroup of Cohort A Participants with PFI/TFI >6-12 Months |
| End point description: | |
| OS was defined as the time from the first dose of study drug to death due to any cause. OS was analyzed by KM method and is reported as Median OS with a 95% CI. The analysis population included a subgroup of participants in Cohort A who had a PFI/TFI (duration from end of treatment to disease recurrence) >6-12 months and received \geq 1 dose of study drug. Per protocol PFI/TFI >6-12 months subgroup analysis of OS was not planned or executed in Cohort B. | |
| End point type | Secondary |
| End point timeframe: | |
| Up to ~43 months (through database cut-off date of 18-September-2019) | |

| | | | | |
|----------------------------------|---|--|--|--|
| End point values | Cohort A Participants with PFI/TFI >6-12 Months | | | |
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 115 | | | |
| Units: Months | | | | |
| median (confidence interval 95%) | 22.1 (15.2 to 27.9) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with OS (OS Rate) at Month 6 in Subgroup of Cohort A Participants with PFI/TFI >6-12 Months

| | |
|-----------------|--|
| End point title | Percentage of Participants with OS (OS Rate) at Month 6 in Subgroup of Cohort A Participants with PFI/TFI >6-12 Months |
|-----------------|--|

End point description:

OS was defined as the time from the first dose of study drug to death due to any cause. The percentage of participants with OS (OS rate) at Month 6 is reported. The analysis population included a subgroup of participants in Cohort A who had a PFI/TFI (duration from end of treatment to disease recurrence) >6-12 months and received ≥ 1 dose of study drug. Per protocol PFI/TFI >6-12 months subgroup analysis of OS rate at Month 6 was not planned or executed in Cohort B.

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

End point timeframe:

Month 6

| | | | | |
|-----------------------------------|---|--|--|--|
| End point values | Cohort A Participants with PFI/TFI >6-12 Months | | | |
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 115 | | | |
| Units: Percentage of Participants | | | | |
| number (confidence interval 95%) | 86.1 (78.3 to 91.2) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with OS (OS Rate) at Month 12 in Subgroup of Cohort A Participants with PFI/TFI >6-12 Months

| | |
|-----------------|---|
| End point title | Percentage of Participants with OS (OS Rate) at Month 12 in Subgroup of Cohort A Participants with PFI/TFI >6-12 Months |
|-----------------|---|

End point description:

OS was defined as the time from the first dose of study drug to death due to any cause. The percentage of participants with OS (OS rate) at Month 12 is reported. The analysis population included a subgroup of participants in Cohort A who had a PFI/TFI (duration from end of treatment to disease recurrence) >6-12 months and received ≥ 1 dose of study drug. Per protocol PFI/TFI >6-12 months subgroup analysis of OS rate at Month 12 was not planned or executed in Cohort B.

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

End point timeframe:

Month 12

| End point values | Cohort A Participants with PFI/TFI >6-12 Months | | | |
|-----------------------------------|--|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 115 | | | |
| Units: Percentage of Participants | | | | |
| number (confidence interval 95%) | 68.7 (59.3 to 76.3) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with OS (OS Rate) at Month 18 in Subgroup of Cohort A Participants with PFI/TFI >6-12 Months

| | |
|-----------------|---|
| End point title | Percentage of Participants with OS (OS Rate) at Month 18 in Subgroup of Cohort A Participants with PFI/TFI >6-12 Months |
|-----------------|---|

End point description:

OS was defined as the time from the first dose of study drug to death due to any cause. The percentage of participants with OS (OS rate) at Month 18 is reported. The analysis population included a subgroup of participants in Cohort A who had a PFI/TFI (duration from end of treatment to disease recurrence) >6-12 months and received ≥ 1 dose of study drug. Per protocol PFI/TFI >6-12 months subgroup analysis of OS rate at Month 18 was not planned or executed in Cohort B.

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

End point timeframe:

Month 18

| End point values | Cohort A Participants with PFI/TFI >6-12 Months | | | |
|-----------------------------------|--|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 115 | | | |
| Units: Percentage of Participants | | | | |
| number (confidence interval 95%) | 54.6 (45.0 to 63.2) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants Who Experienced an Adverse Event (AE)

| | |
|-----------------|--|
| End point title | Number of Participants Who Experienced an Adverse Event (AE) |
|-----------------|--|

End point description:

An AE was defined as any untoward medical occurrence in a pharmaceutical product which does not necessarily have to have a causal relationship with this treatment. An AE could therefore be any unfavorable and unintended sign, symptom, or disease temporally associated with the use of a medicinal product or protocol-specified procedure, whether or not considered related to the medicinal product or protocol-specified procedure. Any worsening of a pre-existing condition that was temporally associated with the use of the Sponsor's product was also an AE. As specified by the protocol, the number of participants who experienced at least one AE is reported here for all participants in Cohort A and Cohort B who received ≥ 1 dose of study drug.

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

End point timeframe:

Up to ~58.8 months (through database cut-off date of 18-March-2021)

| End point values | Cohort A: Pembrolizumab | Cohort B: Pembrolizumab | | |
|-----------------------------|----------------------------|----------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 285 | 91 | | |
| Units: Participants | 274 | 85 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants Who Discontinued Study Treatment due to an AE

| | |
|-----------------|--|
| End point title | Number of Participants Who Discontinued Study Treatment due to an AE |
|-----------------|--|

End point description:

An AE was defined as any untoward medical occurrence in a pharmaceutical product which does not necessarily have to have a causal relationship with this treatment. An AE could therefore be any unfavorable and unintended sign, symptom, or disease temporally associated with the use of a medicinal product or protocol-specified procedure, whether or not considered related to the medicinal product or protocol-specified procedure. Any worsening of a pre-existing condition that was temporally associated with the use of the Sponsor's product was also an AE. As specified by the protocol, the number of participants who discontinued study treatment due to an AE is reported here for all participants in Cohort A and Cohort B who received ≥ 1 dose of study drug.

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

End point timeframe:

Up to ~58.8 months (through database cut-off date of 18-March-2021)

| End point values | Cohort A: Pembrolizumab | Cohort B: Pembrolizumab | | |
|-----------------------------|----------------------------|----------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 285 | 91 | | |
| Units: Participants | 23 | 4 | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to approximately 58.8 months (based on the database cut-off date of 18-March-2021)

Adverse event reporting additional description:

All participants who received ≥ 1 dose of study drug. Per protocol, Medical Dictionary for Regulatory Activities (MedDRA) preferred terms "Neoplasm progression (NP)", "Malignant NP" and "Disease progression" considered not related to study drug are excluded as AEs. Second course pembrolizumab AEs are presented separately per protocol.

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

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|------|
| Dictionary version | 23.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|-------------------------|
| Reporting group title | Cohort A: Pembrolizumab |
|-----------------------|-------------------------|

Reporting group description:

Participants in Cohort A received 0-2 prior lines of treatment for recurrent ovarian cancer (ROC; 1-3 total prior lines including front-line treatment) and were administered pembrolizumab at a dose of 200 mg via intravenous (IV) infusion on Day 1 of each 21-day cycle for up to 35 cycles (up to ~2 years). Qualified participants who complete 35 administrations of pembrolizumab but progress after discontinuation can initiate a second course of pembrolizumab 200 mg for up to 17 cycles (up to ~1 additional year).

| | |
|-----------------------|-------------------------|
| Reporting group title | Cohort B: Pembrolizumab |
|-----------------------|-------------------------|

Reporting group description:

Participants in Cohort B received 3-5 prior lines of treatment for ROC (4-6 total prior lines including front-line treatment) and were administered pembrolizumab at a dose of 200 mg via IV infusion on Day 1 of each 21-day cycle for up to 35 cycles (up to ~2 years). Qualified participants who complete 35 administrations of pembrolizumab but progress after discontinuation can initiate a second course of pembrolizumab 200 mg for up to 17 cycles (up to ~1 additional year).

| | |
|-----------------------|---------------------------------------|
| Reporting group title | Cohort A: Second Course Pembrolizumab |
|-----------------------|---------------------------------------|

Reporting group description:

Eligible participants in Cohort A who stopped pembrolizumab with stable disease (SD) or better but progressed after stopping study treatment initiated a second course of pembrolizumab at the investigator's discretion at the same dose and schedule (200 mg Q3W) for up to 17 cycles (up to approximately 1 additional year).

| | |
|-----------------------|---------------------------------------|
| Reporting group title | Cohort B: Second Course Pembrolizumab |
|-----------------------|---------------------------------------|

Reporting group description:

Eligible participants in Cohort B who stopped pembrolizumab with SD or better but progressed after stopping study treatment initiated a second course of pembrolizumab at the investigator's discretion at the same dose and schedule (200 mg Q3W) for up to 17 cycles (up to approximately 1 additional year).

| Serious adverse events | Cohort A: Pembrolizumab | Cohort B: Pembrolizumab | Cohort A: Second Course Pembrolizumab |
|---|----------------------------|----------------------------|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 91 / 285 (31.93%) | 26 / 91 (28.57%) | 1 / 5 (20.00%) |
| number of deaths (all causes) | 233 | 77 | 1 |
| number of deaths resulting from adverse events | 2 | 0 | 0 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |

| | | | |
|---|-----------------|----------------|---------------|
| Cancer pain | | | |
| subjects affected / exposed | 2 / 285 (0.70%) | 0 / 91 (0.00%) | 0 / 5 (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 |
| Infected neoplasm | | | |
| subjects affected / exposed | 1 / 285 (0.35%) | 0 / 91 (0.00%) | 0 / 5 (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 |
| Malignant ascites | | | |
| subjects affected / exposed | 1 / 285 (0.35%) | 0 / 91 (0.00%) | 0 / 5 (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 |
| Paraneoplastic syndrome | | | |
| subjects affected / exposed | 1 / 285 (0.35%) | 0 / 91 (0.00%) | 0 / 5 (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 |
| Tumour associated fever | | | |
| subjects affected / exposed | 1 / 285 (0.35%) | 0 / 91 (0.00%) | 0 / 5 (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 |
| Vascular disorders | | | |
| Circulatory collapse | | | |
| subjects affected / exposed | 1 / 285 (0.35%) | 0 / 91 (0.00%) | 0 / 5 (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 |
| Deep vein thrombosis | | | |
| subjects affected / exposed | 2 / 285 (0.70%) | 0 / 91 (0.00%) | 0 / 5 (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 |
| Embolism | | | |
| subjects affected / exposed | 0 / 285 (0.00%) | 1 / 91 (1.10%) | 0 / 5 (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 |
| Hypotension | | | |

| | | | |
|--|-----------------|----------------|---------------|
| subjects affected / exposed | 0 / 285 (0.00%) | 1 / 91 (1.10%) | 0 / 5 (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 |
| Vena cava embolism | | | |
| subjects affected / exposed | 1 / 285 (0.35%) | 0 / 91 (0.00%) | 0 / 5 (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 |
| Vena cava thrombosis | | | |
| subjects affected / exposed | 1 / 285 (0.35%) | 0 / 91 (0.00%) | 0 / 5 (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 |
| General disorders and administration site conditions | | | |
| Death | | | |
| subjects affected / exposed | 2 / 285 (0.70%) | 0 / 91 (0.00%) | 0 / 5 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| General physical health deterioration | | | |
| subjects affected / exposed | 2 / 285 (0.70%) | 0 / 91 (0.00%) | 0 / 5 (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 |
| Incarcerated hernia | | | |
| subjects affected / exposed | 1 / 285 (0.35%) | 0 / 91 (0.00%) | 0 / 5 (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 |
| Pyrexia | | | |
| subjects affected / exposed | 1 / 285 (0.35%) | 1 / 91 (1.10%) | 0 / 5 (0.00%) |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Immune system disorders | | | |
| Drug hypersensitivity | | | |
| subjects affected / exposed | 2 / 285 (0.70%) | 0 / 91 (0.00%) | 0 / 5 (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 |

| | | | |
|---|-----------------|----------------|---------------|
| Sarcoidosis | | | |
| subjects affected / exposed | 1 / 285 (0.35%) | 0 / 91 (0.00%) | 0 / 5 (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 |
| Reproductive system and breast disorders | | | |
| Female genital tract fistula | | | |
| subjects affected / exposed | 1 / 285 (0.35%) | 1 / 91 (1.10%) | 0 / 5 (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 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Dyspnoea | | | |
| subjects affected / exposed | 3 / 285 (1.05%) | 0 / 91 (0.00%) | 0 / 5 (0.00%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Haemoptysis | | | |
| subjects affected / exposed | 1 / 285 (0.35%) | 0 / 91 (0.00%) | 0 / 5 (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 |
| Pleural effusion | | | |
| subjects affected / exposed | 7 / 285 (2.46%) | 0 / 91 (0.00%) | 0 / 5 (0.00%) |
| occurrences causally related to treatment / all | 1 / 8 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| Pleurisy | | | |
| subjects affected / exposed | 1 / 285 (0.35%) | 0 / 91 (0.00%) | 0 / 5 (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 |
| Pneumonitis | | | |
| subjects affected / exposed | 2 / 285 (0.70%) | 0 / 91 (0.00%) | 0 / 5 (0.00%) |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary embolism | | | |

| | | | |
|---|-----------------|----------------|----------------|
| subjects affected / exposed | 3 / 285 (1.05%) | 1 / 91 (1.10%) | 0 / 5 (0.00%) |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| Dyspnoea at rest | | | |
| subjects affected / exposed | 0 / 285 (0.00%) | 0 / 91 (0.00%) | 1 / 5 (20.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Psychiatric disorders | | | |
| Anxiety | | | |
| subjects affected / exposed | 0 / 285 (0.00%) | 1 / 91 (1.10%) | 0 / 5 (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 |
| Suicide attempt | | | |
| subjects affected / exposed | 1 / 285 (0.35%) | 0 / 91 (0.00%) | 0 / 5 (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 |
| Product issues | | | |
| Device malfunction | | | |
| subjects affected / exposed | 1 / 285 (0.35%) | 0 / 91 (0.00%) | 0 / 5 (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 |
| Investigations | | | |
| Blood bilirubin increased | | | |
| subjects affected / exposed | 1 / 285 (0.35%) | 0 / 91 (0.00%) | 0 / 5 (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 |
| Blood sodium decreased | | | |
| subjects affected / exposed | 1 / 285 (0.35%) | 0 / 91 (0.00%) | 0 / 5 (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 |
| Neutrophil count decreased | | | |
| subjects affected / exposed | 1 / 285 (0.35%) | 0 / 91 (0.00%) | 0 / 5 (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 |

| | | | |
|---|-----------------|----------------|---------------|
| Injury, poisoning and procedural complications | | | |
| Gastrointestinal injury | | | |
| subjects affected / exposed | 1 / 285 (0.35%) | 0 / 91 (0.00%) | 0 / 5 (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 |
| Incisional hernia | | | |
| subjects affected / exposed | 1 / 285 (0.35%) | 0 / 91 (0.00%) | 0 / 5 (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 |
| Tibia fracture | | | |
| subjects affected / exposed | 1 / 285 (0.35%) | 0 / 91 (0.00%) | 0 / 5 (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 |
| Nervous system disorders | | | |
| Cerebral infarction | | | |
| subjects affected / exposed | 1 / 285 (0.35%) | 0 / 91 (0.00%) | 0 / 5 (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 |
| Intercostal neuralgia | | | |
| subjects affected / exposed | 0 / 285 (0.00%) | 1 / 91 (1.10%) | 0 / 5 (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 |
| Myasthenic syndrome | | | |
| subjects affected / exposed | 1 / 285 (0.35%) | 0 / 91 (0.00%) | 0 / 5 (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 |
| Blood and lymphatic system disorders | | | |
| Splenic haematoma | | | |
| subjects affected / exposed | 1 / 285 (0.35%) | 0 / 91 (0.00%) | 0 / 5 (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 |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |

| | | | |
|---|-----------------|----------------|---------------|
| subjects affected / exposed | 1 / 285 (0.35%) | 0 / 91 (0.00%) | 0 / 5 (0.00%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ascites | | | |
| subjects affected / exposed | 9 / 285 (3.16%) | 2 / 91 (2.20%) | 0 / 5 (0.00%) |
| occurrences causally related to treatment / all | 0 / 12 | 1 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Autoimmune colitis | | | |
| subjects affected / exposed | 1 / 285 (0.35%) | 0 / 91 (0.00%) | 0 / 5 (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 |
| Colitis | | | |
| subjects affected / exposed | 3 / 285 (1.05%) | 2 / 91 (2.20%) | 0 / 5 (0.00%) |
| occurrences causally related to treatment / all | 3 / 3 | 1 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Colonic fistula | | | |
| subjects affected / exposed | 0 / 285 (0.00%) | 1 / 91 (1.10%) | 0 / 5 (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 |
| Constipation | | | |
| subjects affected / exposed | 2 / 285 (0.70%) | 0 / 91 (0.00%) | 0 / 5 (0.00%) |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diarrhoea | | | |
| subjects affected / exposed | 3 / 285 (1.05%) | 1 / 91 (1.10%) | 0 / 5 (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 |
| Duodenal ulcer | | | |
| subjects affected / exposed | 1 / 285 (0.35%) | 0 / 91 (0.00%) | 0 / 5 (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 |
| Enteritis | | | |

| | | | |
|---|-----------------|----------------|---------------|
| subjects affected / exposed | 1 / 285 (0.35%) | 1 / 91 (1.10%) | 0 / 5 (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 |
| Gastrointestinal disorder | | | |
| subjects affected / exposed | 1 / 285 (0.35%) | 0 / 91 (0.00%) | 0 / 5 (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 |
| Gastrointestinal perforation | | | |
| subjects affected / exposed | 1 / 285 (0.35%) | 0 / 91 (0.00%) | 0 / 5 (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 |
| Haematemesis | | | |
| subjects affected / exposed | 1 / 285 (0.35%) | 0 / 91 (0.00%) | 0 / 5 (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 |
| Ileus | | | |
| subjects affected / exposed | 5 / 285 (1.75%) | 1 / 91 (1.10%) | 0 / 5 (0.00%) |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Intestinal obstruction | | | |
| subjects affected / exposed | 4 / 285 (1.40%) | 0 / 91 (0.00%) | 0 / 5 (0.00%) |
| occurrences causally related to treatment / all | 0 / 6 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Intussusception | | | |
| subjects affected / exposed | 1 / 285 (0.35%) | 0 / 91 (0.00%) | 0 / 5 (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 |
| Large intestinal haemorrhage | | | |
| subjects affected / exposed | 1 / 285 (0.35%) | 0 / 91 (0.00%) | 0 / 5 (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 |
| Large intestinal obstruction | | | |

| | | | |
|---|------------------|----------------|---------------|
| subjects affected / exposed | 1 / 285 (0.35%) | 0 / 91 (0.00%) | 0 / 5 (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 |
| Large intestine perforation | | | |
| subjects affected / exposed | 1 / 285 (0.35%) | 0 / 91 (0.00%) | 0 / 5 (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 |
| Oesophageal ulcer | | | |
| subjects affected / exposed | 1 / 285 (0.35%) | 0 / 91 (0.00%) | 0 / 5 (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 |
| Proctalgia | | | |
| subjects affected / exposed | 0 / 285 (0.00%) | 1 / 91 (1.10%) | 0 / 5 (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 |
| Rectal haemorrhage | | | |
| subjects affected / exposed | 2 / 285 (0.70%) | 0 / 91 (0.00%) | 0 / 5 (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 |
| Small intestinal obstruction | | | |
| subjects affected / exposed | 10 / 285 (3.51%) | 1 / 91 (1.10%) | 0 / 5 (0.00%) |
| occurrences causally related to treatment / all | 0 / 14 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Subileus | | | |
| subjects affected / exposed | 2 / 285 (0.70%) | 2 / 91 (2.20%) | 0 / 5 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vomiting | | | |
| subjects affected / exposed | 3 / 285 (1.05%) | 1 / 91 (1.10%) | 0 / 5 (0.00%) |
| occurrences causally related to treatment / all | 1 / 3 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatobiliary disorders | | | |
| Budd-Chiari syndrome | | | |

| | | | |
|---|-----------------|----------------|---------------|
| subjects affected / exposed | 0 / 285 (0.00%) | 1 / 91 (1.10%) | 0 / 5 (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 |
| Hepatotoxicity | | | |
| subjects affected / exposed | 0 / 285 (0.00%) | 1 / 91 (1.10%) | 0 / 5 (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 |
| Portal vein thrombosis | | | |
| subjects affected / exposed | 1 / 285 (0.35%) | 0 / 91 (0.00%) | 0 / 5 (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 |
| Biliary obstruction | | | |
| subjects affected / exposed | 1 / 285 (0.35%) | 0 / 91 (0.00%) | 0 / 5 (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 |
| Skin and subcutaneous tissue disorders | | | |
| Dermatitis | | | |
| subjects affected / exposed | 1 / 285 (0.35%) | 0 / 91 (0.00%) | 0 / 5 (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 |
| Perivascular dermatitis | | | |
| subjects affected / exposed | 1 / 285 (0.35%) | 0 / 91 (0.00%) | 0 / 5 (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 |
| Rash | | | |
| subjects affected / exposed | 0 / 285 (0.00%) | 1 / 91 (1.10%) | 0 / 5 (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 |
| Stevens-Johnson syndrome | | | |
| subjects affected / exposed | 1 / 285 (0.35%) | 0 / 91 (0.00%) | 0 / 5 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| Renal and urinary disorders | | | |

| | | | |
|---|-----------------|----------------|---------------|
| Acute kidney injury | | | |
| subjects affected / exposed | 2 / 285 (0.70%) | 2 / 91 (2.20%) | 0 / 5 (0.00%) |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hydronephrosis | | | |
| subjects affected / exposed | 0 / 285 (0.00%) | 1 / 91 (1.10%) | 0 / 5 (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 |
| Hydroureter | | | |
| subjects affected / exposed | 0 / 285 (0.00%) | 1 / 91 (1.10%) | 0 / 5 (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 |
| Renal failure | | | |
| subjects affected / exposed | 1 / 285 (0.35%) | 0 / 91 (0.00%) | 0 / 5 (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 |
| Tubulointerstitial nephritis | | | |
| subjects affected / exposed | 1 / 285 (0.35%) | 0 / 91 (0.00%) | 0 / 5 (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 |
| Endocrine disorders | | | |
| Addison's disease | | | |
| subjects affected / exposed | 1 / 285 (0.35%) | 0 / 91 (0.00%) | 0 / 5 (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 |
| Adrenal insufficiency | | | |
| subjects affected / exposed | 1 / 285 (0.35%) | 0 / 91 (0.00%) | 0 / 5 (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 |
| Hypoaldosteronism | | | |
| subjects affected / exposed | 1 / 285 (0.35%) | 0 / 91 (0.00%) | 0 / 5 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| Hypophysitis | | | |

| | | | |
|---|-----------------|----------------|---------------|
| subjects affected / exposed | 1 / 285 (0.35%) | 0 / 91 (0.00%) | 0 / 5 (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 |
| Hypothyroidism | | | |
| subjects affected / exposed | 1 / 285 (0.35%) | 0 / 91 (0.00%) | 0 / 5 (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 |
| Lymphocytic hypophysitis | | | |
| subjects affected / exposed | 1 / 285 (0.35%) | 0 / 91 (0.00%) | 0 / 5 (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 |
| Infections and infestations | | | |
| Acinetobacter infection | | | |
| subjects affected / exposed | 0 / 285 (0.00%) | 1 / 91 (1.10%) | 0 / 5 (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 |
| Bacterial sepsis | | | |
| subjects affected / exposed | 1 / 285 (0.35%) | 1 / 91 (1.10%) | 0 / 5 (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 |
| Cellulitis | | | |
| subjects affected / exposed | 1 / 285 (0.35%) | 0 / 91 (0.00%) | 0 / 5 (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 |
| Clostridium difficile colitis | | | |
| subjects affected / exposed | 1 / 285 (0.35%) | 0 / 91 (0.00%) | 0 / 5 (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 |
| Clostridium difficile infection | | | |
| subjects affected / exposed | 0 / 285 (0.00%) | 1 / 91 (1.10%) | 0 / 5 (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 |
| Gastroenteritis | | | |

| | | | |
|---|-----------------|----------------|---------------|
| subjects affected / exposed | 1 / 285 (0.35%) | 0 / 91 (0.00%) | 0 / 5 (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 |
| Herpes virus infection | | | |
| subjects affected / exposed | 1 / 285 (0.35%) | 0 / 91 (0.00%) | 0 / 5 (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 |
| Herpes zoster | | | |
| subjects affected / exposed | 1 / 285 (0.35%) | 0 / 91 (0.00%) | 0 / 5 (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 | | | |
| subjects affected / exposed | 1 / 285 (0.35%) | 0 / 91 (0.00%) | 0 / 5 (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 |
| Laryngitis | | | |
| subjects affected / exposed | 1 / 285 (0.35%) | 0 / 91 (0.00%) | 0 / 5 (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 |
| Peritonitis | | | |
| subjects affected / exposed | 1 / 285 (0.35%) | 1 / 91 (1.10%) | 0 / 5 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pharyngitis streptococcal | | | |
| subjects affected / exposed | 1 / 285 (0.35%) | 0 / 91 (0.00%) | 0 / 5 (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 |
| Pleural infection bacterial | | | |
| subjects affected / exposed | 1 / 285 (0.35%) | 0 / 91 (0.00%) | 0 / 5 (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 | 4 / 285 (1.40%) | 1 / 91 (1.10%) | 1 / 5 (20.00%) |
| occurrences causally related to treatment / all | 2 / 5 | 0 / 2 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Post procedural infection | | | |
| subjects affected / exposed | 1 / 285 (0.35%) | 0 / 91 (0.00%) | 0 / 5 (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 |
| Pyelonephritis acute | | | |
| subjects affected / exposed | 1 / 285 (0.35%) | 0 / 91 (0.00%) | 0 / 5 (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 |
| Sepsis | | | |
| subjects affected / exposed | 1 / 285 (0.35%) | 1 / 91 (1.10%) | 0 / 5 (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 |
| Sepsis syndrome | | | |
| subjects affected / exposed | 0 / 285 (0.00%) | 1 / 91 (1.10%) | 0 / 5 (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 |
| Urinary tract infection | | | |
| subjects affected / exposed | 1 / 285 (0.35%) | 2 / 91 (2.20%) | 0 / 5 (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 |
| Metabolism and nutrition disorders | | | |
| Dehydration | | | |
| subjects affected / exposed | 1 / 285 (0.35%) | 1 / 91 (1.10%) | 0 / 5 (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 |
| Diabetes mellitus | | | |
| subjects affected / exposed | 1 / 285 (0.35%) | 0 / 91 (0.00%) | 0 / 5 (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 |
| Hypercalcaemia | | | |

| | | | |
|---|-----------------|----------------|---------------|
| subjects affected / exposed | 3 / 285 (1.05%) | 0 / 91 (0.00%) | 0 / 5 (0.00%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hyponatraemia | | | |
| subjects affected / exposed | 1 / 285 (0.35%) | 0 / 91 (0.00%) | 0 / 5 (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 |
| Type 1 diabetes mellitus | | | |
| subjects affected / exposed | 1 / 285 (0.35%) | 1 / 91 (1.10%) | 0 / 5 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|---------------------------------------|--|--|
| Serious adverse events | Cohort B: Second Course Pembrolizumab | | |
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | 0 | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Cancer pain | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infected neoplasm | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Malignant ascites | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Paraneoplastic syndrome | | | |

| | | | |
|--|---------------|--|--|
| subjects affected / exposed | 0 / 2 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Tumour associated fever | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Vascular disorders | | | |
| Circulatory collapse | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Deep vein thrombosis | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Embolism | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hypotension | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Vena cava embolism | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Vena cava thrombosis | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| General disorders and administration site conditions | | | |

| | | | |
|---|---------------|--|--|
| Death | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| General physical health deterioration | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Incarcerated hernia | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pyrexia | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Immune system disorders | | | |
| Drug hypersensitivity | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Sarcoidosis | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Reproductive system and breast disorders | | | |
| Female genital tract fistula | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Dyspnoea | | | |

| | | | |
|---|---------------|--|--|
| subjects affected / exposed | 0 / 2 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Haemoptysis | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pleural effusion | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pleurisy | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pneumonitis | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pulmonary embolism | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Dyspnoea at rest | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Psychiatric disorders | | | |
| Anxiety | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Suicide attempt | | | |

| | | | |
|---|---------------|--|--|
| subjects affected / exposed | 0 / 2 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Product issues | | | |
| Device malfunction | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Investigations | | | |
| Blood bilirubin increased | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Blood sodium decreased | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Neutrophil count decreased | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Injury, poisoning and procedural complications | | | |
| Gastrointestinal injury | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Incisional hernia | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Tibia fracture | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | |
|---|---------------|--|--|
| Nervous system disorders | | | |
| Cerebral infarction | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Intercostal neuralgia | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Myasthenic syndrome | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Blood and lymphatic system disorders | | | |
| Splenic haematoma | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Ascites | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Autoimmune colitis | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Colitis | | | |

| | | | | |
|---|---------------|--|--|--|
| subjects affected / exposed | 0 / 2 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Colonic fistula | | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Constipation | | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Diarrhoea | | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Duodenal ulcer | | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Enteritis | | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Gastrointestinal disorder | | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Gastrointestinal perforation | | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Haematemesis | | | | |

| | | | | |
|---|---------------|--|--|--|
| subjects affected / exposed | 0 / 2 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Ileus | | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Intestinal obstruction | | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Intussusception | | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Large intestinal haemorrhage | | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Large intestinal obstruction | | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Large intestine perforation | | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Oesophageal ulcer | | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Proctalgia | | | | |

| | | | |
|---|---------------|--|--|
| subjects affected / exposed | 0 / 2 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Rectal haemorrhage | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Small intestinal obstruction | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Subileus | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Vomiting | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hepatobiliary disorders | | | |
| Budd-Chiari syndrome | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hepatotoxicity | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Portal vein thrombosis | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Biliary obstruction | | | |

| | | | |
|---|---------------|--|--|
| subjects affected / exposed | 0 / 2 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Skin and subcutaneous tissue disorders | | | |
| Dermatitis | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Perivascular dermatitis | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Rash | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Stevens-Johnson syndrome | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Renal and urinary disorders | | | |
| Acute kidney injury | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hydronephrosis | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hydroureter | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Renal failure | | | |

| | | | |
|---|---------------|--|--|
| subjects affected / exposed | 0 / 2 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Tubulointerstitial nephritis | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Endocrine disorders | | | |
| Addison's disease | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Adrenal insufficiency | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hypoaldosteronism | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hypophysitis | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hypothyroidism | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Lymphocytic hypophysitis | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infections and infestations | | | |

| | | | | |
|---|---------------|--|--|--|
| Acinetobacter infection | | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Bacterial sepsis | | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Cellulitis | | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Clostridium difficile colitis | | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Clostridium difficile infection | | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Gastroenteritis | | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Herpes virus infection | | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Herpes zoster | | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Influenza | | | | |

| | | | | |
|---|---------------|--|--|--|
| subjects affected / exposed | 0 / 2 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Laryngitis | | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Peritonitis | | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pharyngitis streptococcal | | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pleural infection bacterial | | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pneumonia | | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Post procedural infection | | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pyelonephritis acute | | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Sepsis | | | | |

| | | | |
|---|---------------|--|--|
| subjects affected / exposed | 0 / 2 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Sepsis syndrome | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Urinary tract infection | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Metabolism and nutrition disorders | | | |
| Dehydration | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Diabetes mellitus | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hypercalcaemia | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hyponatraemia | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Type 1 diabetes mellitus | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

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

| Non-serious adverse events | Cohort A: Pembrolizumab | Cohort B: Pembrolizumab | Cohort A: Second Course Pembrolizumab |
|---|------------------------------------|------------------------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 272 / 285 (95.44%) | 84 / 91 (92.31%) | 5 / 5 (100.00%) |
| Vascular disorders | | | |
| Aortic aneurysm | | | |
| subjects affected / exposed | 0 / 285 (0.00%) | 0 / 91 (0.00%) | 1 / 5 (20.00%) |
| occurrences (all) | 0 | 0 | 1 |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 45 / 285 (15.79%) | 26 / 91 (28.57%) | 0 / 5 (0.00%) |
| occurrences (all) | 52 | 29 | 0 |
| Fatigue | | | |
| subjects affected / exposed | 96 / 285 (33.68%) | 22 / 91 (24.18%) | 1 / 5 (20.00%) |
| occurrences (all) | 118 | 27 | 2 |
| Oedema peripheral | | | |
| subjects affected / exposed | 22 / 285 (7.72%) | 4 / 91 (4.40%) | 0 / 5 (0.00%) |
| occurrences (all) | 30 | 4 | 0 |
| Pain | | | |
| subjects affected / exposed | 2 / 285 (0.70%) | 5 / 91 (5.49%) | 0 / 5 (0.00%) |
| occurrences (all) | 2 | 5 | 0 |
| Pyrexia | | | |
| subjects affected / exposed | 31 / 285 (10.88%) | 9 / 91 (9.89%) | 0 / 5 (0.00%) |
| occurrences (all) | 37 | 11 | 0 |
| Hernia | | | |
| subjects affected / exposed | 0 / 285 (0.00%) | 1 / 91 (1.10%) | 0 / 5 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Suprapubic pain | | | |
| subjects affected / exposed | 0 / 285 (0.00%) | 0 / 91 (0.00%) | 1 / 5 (20.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough | | | |
| subjects affected / exposed | 38 / 285 (13.33%) | 13 / 91 (14.29%) | 0 / 5 (0.00%) |
| occurrences (all) | 44 | 14 | 0 |

| | | | |
|---|-------------------|----------------|----------------|
| Dyspnoea | | | |
| subjects affected / exposed | 40 / 285 (14.04%) | 6 / 91 (6.59%) | 0 / 5 (0.00%) |
| occurrences (all) | 49 | 8 | 0 |
| Haemoptysis | | | |
| subjects affected / exposed | 0 / 285 (0.00%) | 0 / 91 (0.00%) | 1 / 5 (20.00%) |
| occurrences (all) | 0 | 0 | 2 |
| Productive cough | | | |
| subjects affected / exposed | 7 / 285 (2.46%) | 1 / 91 (1.10%) | 1 / 5 (20.00%) |
| occurrences (all) | 8 | 1 | 1 |
| Sputum discoloured | | | |
| subjects affected / exposed | 0 / 285 (0.00%) | 0 / 91 (0.00%) | 1 / 5 (20.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Psychiatric disorders | | | |
| Insomnia | | | |
| subjects affected / exposed | 17 / 285 (5.96%) | 3 / 91 (3.30%) | 1 / 5 (20.00%) |
| occurrences (all) | 19 | 4 | 1 |
| Investigations | | | |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 17 / 285 (5.96%) | 1 / 91 (1.10%) | 1 / 5 (20.00%) |
| occurrences (all) | 19 | 1 | 1 |
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 19 / 285 (6.67%) | 2 / 91 (2.20%) | 0 / 5 (0.00%) |
| occurrences (all) | 21 | 2 | 0 |
| Blood alkaline phosphatase increased | | | |
| subjects affected / exposed | 19 / 285 (6.67%) | 3 / 91 (3.30%) | 1 / 5 (20.00%) |
| occurrences (all) | 23 | 3 | 1 |
| Weight decreased | | | |
| subjects affected / exposed | 17 / 285 (5.96%) | 6 / 91 (6.59%) | 0 / 5 (0.00%) |
| occurrences (all) | 17 | 6 | 0 |
| Activated partial thromboplastin time prolonged | | | |
| subjects affected / exposed | 0 / 285 (0.00%) | 0 / 91 (0.00%) | 1 / 5 (20.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Blood bicarbonate increased | | | |
| subjects affected / exposed | 0 / 285 (0.00%) | 0 / 91 (0.00%) | 1 / 5 (20.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Blood lactate dehydrogenase | | | |

| | | | |
|--|-------------------|------------------|----------------|
| increased | | | |
| subjects affected / exposed | 7 / 285 (2.46%) | 1 / 91 (1.10%) | 1 / 5 (20.00%) |
| occurrences (all) | 7 | 1 | 1 |
| PCO2 increased | | | |
| subjects affected / exposed | 0 / 285 (0.00%) | 0 / 91 (0.00%) | 1 / 5 (20.00%) |
| occurrences (all) | 0 | 0 | 1 |
| White blood cells urine positive | | | |
| subjects affected / exposed | 0 / 285 (0.00%) | 0 / 91 (0.00%) | 1 / 5 (20.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Injury, poisoning and procedural complications | | | |
| Bone contusion | | | |
| subjects affected / exposed | 0 / 285 (0.00%) | 0 / 91 (0.00%) | 1 / 5 (20.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Incision site complication | | | |
| subjects affected / exposed | 0 / 285 (0.00%) | 0 / 91 (0.00%) | 1 / 5 (20.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Nervous system disorders | | | |
| Dizziness | | | |
| subjects affected / exposed | 21 / 285 (7.37%) | 6 / 91 (6.59%) | 0 / 5 (0.00%) |
| occurrences (all) | 22 | 6 | 0 |
| Headache | | | |
| subjects affected / exposed | 25 / 285 (8.77%) | 9 / 91 (9.89%) | 1 / 5 (20.00%) |
| occurrences (all) | 32 | 11 | 2 |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 40 / 285 (14.04%) | 13 / 91 (14.29%) | 0 / 5 (0.00%) |
| occurrences (all) | 58 | 18 | 0 |
| Lymph node pain | | | |
| subjects affected / exposed | 0 / 285 (0.00%) | 0 / 91 (0.00%) | 1 / 5 (20.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Eye disorders | | | |
| Eyelid rash | | | |
| subjects affected / exposed | 0 / 285 (0.00%) | 0 / 91 (0.00%) | 1 / 5 (20.00%) |
| occurrences (all) | 0 | 0 | 3 |
| Eyelids pruritus | | | |

| | | | |
|--|----------------------|---------------------|---------------------|
| subjects affected / exposed occurrences (all) | 0 / 285 (0.00%) 0 | 0 / 91 (0.00%) 0 | 1 / 5 (20.00%) 3 |
| Gastrointestinal disorders | | | |
| Abdominal distension | | | |
| subjects affected / exposed | 20 / 285 (7.02%) | 5 / 91 (5.49%) | 1 / 5 (20.00%) |
| occurrences (all) | 24 | 5 | 2 |
| Abdominal pain | | | |
| subjects affected / exposed | 76 / 285 (26.67%) | 20 / 91 (21.98%) | 0 / 5 (0.00%) |
| occurrences (all) | 90 | 26 | 0 |
| Abdominal pain upper | | | |
| subjects affected / exposed | 17 / 285 (5.96%) | 8 / 91 (8.79%) | 0 / 5 (0.00%) |
| occurrences (all) | 19 | 9 | 0 |
| Ascites | | | |
| subjects affected / exposed | 31 / 285 (10.88%) | 7 / 91 (7.69%) | 0 / 5 (0.00%) |
| occurrences (all) | 47 | 7 | 0 |
| Constipation | | | |
| subjects affected / exposed | 59 / 285 (20.70%) | 22 / 91 (24.18%) | 0 / 5 (0.00%) |
| occurrences (all) | 63 | 25 | 0 |
| Diarrhoea | | | |
| subjects affected / exposed | 56 / 285 (19.65%) | 20 / 91 (21.98%) | 2 / 5 (40.00%) |
| occurrences (all) | 85 | 30 | 2 |
| Dry mouth | | | |
| subjects affected / exposed | 15 / 285 (5.26%) | 2 / 91 (2.20%) | 0 / 5 (0.00%) |
| occurrences (all) | 15 | 2 | 0 |
| Dyspepsia | | | |
| subjects affected / exposed | 18 / 285 (6.32%) | 1 / 91 (1.10%) | 0 / 5 (0.00%) |
| occurrences (all) | 19 | 1 | 0 |
| Nausea | | | |
| subjects affected / exposed | 95 / 285 (33.33%) | 24 / 91 (26.37%) | 1 / 5 (20.00%) |
| occurrences (all) | 123 | 30 | 2 |
| Stomatitis | | | |
| subjects affected / exposed | 14 / 285 (4.91%) | 5 / 91 (5.49%) | 0 / 5 (0.00%) |
| occurrences (all) | 15 | 5 | 0 |
| Vomiting | | | |
| subjects affected / exposed | 61 / 285 (21.40%) | 18 / 91 (19.78%) | 0 / 5 (0.00%) |
| occurrences (all) | 78 | 24 | 0 |

| | | | |
|---|-------------------|------------------|----------------|
| Skin and subcutaneous tissue disorders | | | |
| Dry skin | | | |
| subjects affected / exposed | 15 / 285 (5.26%) | 3 / 91 (3.30%) | 0 / 5 (0.00%) |
| occurrences (all) | 15 | 3 | 0 |
| Pruritus | | | |
| subjects affected / exposed | 31 / 285 (10.88%) | 12 / 91 (13.19%) | 0 / 5 (0.00%) |
| occurrences (all) | 35 | 16 | 0 |
| Rash | | | |
| subjects affected / exposed | 27 / 285 (9.47%) | 8 / 91 (8.79%) | 0 / 5 (0.00%) |
| occurrences (all) | 32 | 11 | 0 |
| Rash maculo-papular | | | |
| subjects affected / exposed | 10 / 285 (3.51%) | 0 / 91 (0.00%) | 1 / 5 (20.00%) |
| occurrences (all) | 13 | 0 | 1 |
| Renal and urinary disorders | | | |
| Dysuria | | | |
| subjects affected / exposed | 5 / 285 (1.75%) | 5 / 91 (5.49%) | 0 / 5 (0.00%) |
| occurrences (all) | 5 | 5 | 0 |
| Endocrine disorders | | | |
| Hyperthyroidism | | | |
| subjects affected / exposed | 19 / 285 (6.67%) | 7 / 91 (7.69%) | 0 / 5 (0.00%) |
| occurrences (all) | 20 | 7 | 0 |
| Hypothyroidism | | | |
| subjects affected / exposed | 33 / 285 (11.58%) | 11 / 91 (12.09%) | 0 / 5 (0.00%) |
| occurrences (all) | 33 | 14 | 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 30 / 285 (10.53%) | 14 / 91 (15.38%) | 1 / 5 (20.00%) |
| occurrences (all) | 33 | 23 | 1 |
| Back pain | | | |
| subjects affected / exposed | 25 / 285 (8.77%) | 10 / 91 (10.99%) | 0 / 5 (0.00%) |
| occurrences (all) | 28 | 14 | 0 |
| Muscle spasms | | | |
| subjects affected / exposed | 8 / 285 (2.81%) | 5 / 91 (5.49%) | 0 / 5 (0.00%) |
| occurrences (all) | 9 | 5 | 0 |
| Myalgia | | | |

| | | | |
|---|-------------------------|------------------------|---------------------|
| subjects affected / exposed occurrences (all) | 19 / 285 (6.67%) 20 | 5 / 91 (5.49%) 5 | 0 / 5 (0.00%) 0 |
| Pain in extremity subjects affected / exposed occurrences (all) | 14 / 285 (4.91%) 19 | 7 / 91 (7.69%) 8 | 0 / 5 (0.00%) 0 |
| Groin pain subjects affected / exposed occurrences (all) | 3 / 285 (1.05%) 3 | 0 / 91 (0.00%) 0 | 1 / 5 (20.00%) 2 |
| Muscular weakness subjects affected / exposed occurrences (all) | 3 / 285 (1.05%) 3 | 0 / 91 (0.00%) 0 | 1 / 5 (20.00%) 1 |
| Infections and infestations | | | |
| Nasopharyngitis subjects affected / exposed occurrences (all) | 16 / 285 (5.61%) 20 | 5 / 91 (5.49%) 6 | 0 / 5 (0.00%) 0 |
| Urinary tract infection subjects affected / exposed occurrences (all) | 21 / 285 (7.37%) 26 | 10 / 91 (10.99%) 13 | 0 / 5 (0.00%) 0 |
| COVID-19 subjects affected / exposed occurrences (all) | 0 / 285 (0.00%) 0 | 0 / 91 (0.00%) 0 | 0 / 5 (0.00%) 0 |
| Sinusitis subjects affected / exposed occurrences (all) | 4 / 285 (1.40%) 4 | 2 / 91 (2.20%) 2 | 1 / 5 (20.00%) 1 |
| Upper respiratory tract infection subjects affected / exposed occurrences (all) | 11 / 285 (3.86%) 12 | 0 / 91 (0.00%) 0 | 1 / 5 (20.00%) 1 |
| Metabolism and nutrition disorders | | | |
| Decreased appetite subjects affected / exposed occurrences (all) | 76 / 285 (26.67%) 84 | 14 / 91 (15.38%) 16 | 0 / 5 (0.00%) 0 |
| Hypomagnesaemia subjects affected / exposed occurrences (all) | 7 / 285 (2.46%) 7 | 6 / 91 (6.59%) 8 | 0 / 5 (0.00%) 0 |
| Hyponatraemia | | | |

| | | | |
|-----------------------------|------------------|----------------|----------------|
| subjects affected / exposed | 10 / 285 (3.51%) | 0 / 91 (0.00%) | 1 / 5 (20.00%) |
| occurrences (all) | 11 | 0 | 4 |
| Hypophosphataemia | | | |
| subjects affected / exposed | 4 / 285 (1.40%) | 2 / 91 (2.20%) | 1 / 5 (20.00%) |
| occurrences (all) | 5 | 6 | 2 |

| | | | |
|---|---------------------------------------|--|--|
| Non-serious adverse events | Cohort B: Second Course Pembrolizumab | | |
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 2 / 2 (100.00%) | | |
| Vascular disorders | | | |
| Aortic aneurysm | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | |
| occurrences (all) | 0 | | |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | |
| occurrences (all) | 0 | | |
| Fatigue | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | |
| occurrences (all) | 0 | | |
| Oedema peripheral | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | |
| occurrences (all) | 0 | | |
| Pain | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | |
| occurrences (all) | 0 | | |
| Pyrexia | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | |
| occurrences (all) | 0 | | |
| Hernia | | | |
| subjects affected / exposed | 1 / 2 (50.00%) | | |
| occurrences (all) | 1 | | |
| Suprapubic pain | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | |
| occurrences (all) | 0 | | |
| Respiratory, thoracic and mediastinal | | | |

| | | | |
|---|----------------|--|--|
| disorders | | | |
| Cough | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | |
| occurrences (all) | 0 | | |
| Dyspnoea | | | |
| subjects affected / exposed | 1 / 2 (50.00%) | | |
| occurrences (all) | 1 | | |
| Haemoptysis | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | |
| occurrences (all) | 0 | | |
| Productive cough | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | |
| occurrences (all) | 0 | | |
| Sputum discoloured | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | |
| occurrences (all) | 0 | | |
| Psychiatric disorders | | | |
| Insomnia | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | |
| occurrences (all) | 0 | | |
| Investigations | | | |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | |
| occurrences (all) | 0 | | |
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | |
| occurrences (all) | 0 | | |
| Blood alkaline phosphatase increased | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | |
| occurrences (all) | 0 | | |
| Weight decreased | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | |
| occurrences (all) | 0 | | |
| Activated partial thromboplastin time prolonged | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | |
| occurrences (all) | 0 | | |

| | | | |
|--|--|--|--|
| Blood bicarbonate increased subjects affected / exposed occurrences (all) | 0 / 2 (0.00%) 0 | | |
| Blood lactate dehydrogenase increased subjects affected / exposed occurrences (all) | 0 / 2 (0.00%) 0 | | |
| PCO2 increased subjects affected / exposed occurrences (all) | 0 / 2 (0.00%) 0 | | |
| White blood cells urine positive subjects affected / exposed occurrences (all) | 0 / 2 (0.00%) 0 | | |
| Injury, poisoning and procedural complications Bone contusion subjects affected / exposed occurrences (all) Incision site complication subjects affected / exposed occurrences (all) | 0 / 2 (0.00%) 0 0 / 2 (0.00%) 0 | | |
| Nervous system disorders Dizziness subjects affected / exposed occurrences (all) Headache subjects affected / exposed occurrences (all) | 0 / 2 (0.00%) 0 0 / 2 (0.00%) 0 | | |
| Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all) Lymph node pain subjects affected / exposed occurrences (all) | 0 / 2 (0.00%) 0 0 / 2 (0.00%) 0 | | |
| Eye disorders Eyelid rash | | | |

| | | | |
|-----------------------------|---------------|--|--|
| subjects affected / exposed | 0 / 2 (0.00%) | | |
| occurrences (all) | 0 | | |
| Eyelids pruritus | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | |
| occurrences (all) | 0 | | |
| Gastrointestinal disorders | | | |
| Abdominal distension | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | |
| occurrences (all) | 0 | | |
| Abdominal pain | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | |
| occurrences (all) | 0 | | |
| Abdominal pain upper | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | |
| occurrences (all) | 0 | | |
| Ascites | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | |
| occurrences (all) | 0 | | |
| Constipation | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | |
| occurrences (all) | 0 | | |
| Diarrhoea | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | |
| occurrences (all) | 0 | | |
| Dry mouth | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | |
| occurrences (all) | 0 | | |
| Dyspepsia | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | |
| occurrences (all) | 0 | | |
| Nausea | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | |
| occurrences (all) | 0 | | |
| Stomatitis | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | |
| occurrences (all) | 0 | | |

| | | | |
|---|--|--|--|
| Vomiting subjects affected / exposed occurrences (all) | 0 / 2 (0.00%) 0 | | |
| Skin and subcutaneous tissue disorders Dry skin subjects affected / exposed occurrences (all) Pruritus subjects affected / exposed occurrences (all) Rash subjects affected / exposed occurrences (all) Rash maculo-papular subjects affected / exposed occurrences (all) | 0 / 2 (0.00%) 0 0 / 2 (0.00%) 0 0 / 2 (0.00%) 0 0 / 2 (0.00%) 0 | | |
| Renal and urinary disorders Dysuria subjects affected / exposed occurrences (all) | 0 / 2 (0.00%) 0 | | |
| Endocrine disorders Hyperthyroidism subjects affected / exposed occurrences (all) Hypothyroidism subjects affected / exposed occurrences (all) | 0 / 2 (0.00%) 0 0 / 2 (0.00%) 0 | | |
| Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) Back pain subjects affected / exposed occurrences (all) Muscle spasms | 0 / 2 (0.00%) 0 0 / 2 (0.00%) 0 | | |

| | | | |
|------------------------------------|----------------|--|--|
| subjects affected / exposed | 0 / 2 (0.00%) | | |
| occurrences (all) | 0 | | |
| Myalgia | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | |
| occurrences (all) | 0 | | |
| Pain in extremity | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | |
| occurrences (all) | 0 | | |
| Groin pain | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | |
| occurrences (all) | 0 | | |
| Muscular weakness | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | |
| occurrences (all) | 0 | | |
| Infections and infestations | | | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | |
| occurrences (all) | 0 | | |
| Urinary tract infection | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | |
| occurrences (all) | 0 | | |
| COVID-19 | | | |
| subjects affected / exposed | 1 / 2 (50.00%) | | |
| occurrences (all) | 1 | | |
| Sinusitis | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | |
| occurrences (all) | 0 | | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | |
| occurrences (all) | 0 | | |
| Metabolism and nutrition disorders | | | |
| Decreased appetite | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | |
| occurrences (all) | 0 | | |
| Hypomagnesaemia | | | |

| | | | |
|-----------------------------|---------------|--|--|
| subjects affected / exposed | 0 / 2 (0.00%) | | |
| occurrences (all) | 0 | | |
| Hyponatraemia | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | |
| occurrences (all) | 0 | | |
| Hypophosphataemia | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | |
| occurrences (all) | 0 | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|------------------|--|
| 19 January 2018 | Amendment 1 expanded on biomarker cutpoint language to provide maximum flexibility to perform additional data analysis, updated language related to pharmacokinetics (PK), and revised guidelines for immune-related adverse events. |
| 21 February 2020 | Amendment 2 added standard pembrolizumab extension study language. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported