Clinical trial results:
An Exploratory Study of the Biologic Effects and Biomarkers of Nivolumab in combination with Ipilimumab in Subjects with Treatment-Naive Stage IV or recurrent Non-Small Cell Lung Cancer (NSCLC) (CheckMate 592: CHECKpoint pathway and nivoluMAb clinical Trial Evaluation 592)

Summary

EudraCT number	2018-000462-11
Trial protocol	DE BE NL ES IT RO
Global end of trial date	24 April 2023

Results information

Result version number	v1 (current)
This version publication date	08 May 2024
First version publication date	08 May 2024

Trial information

Trial identification

Sponsor protocol code	CA209-592

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Bristol-Myers Squibb
Sponsor organisation address	Chaussée de la Hulpe 185, Brussels, Belgium, 1170
Public contact	EU Study Start-Up Unit, Bristol-Myers Squibb International Corporation, Clinical.Trials@bms.com
Scientific contact	Bristol-Myers Squibb Study Director, Bristol-Myers Squibb, Clinical.Trials@bms.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	31 May 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	24 April 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Investigate the biologic effects and biomarkers of nivolumab in combination ipilimumab in subjects, with no prior systemic anticancer therapy given as primary therapy for advanced or metastatic non-small cell lung cancer (NSCLC).

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Conference on Harmonization Good Clinical Practice Guidelines. All the local regulatory requirements pertinent to safety of trial participants were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	29 March 2017
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	Belgium: 18
Country: Number of subjects enrolled	France: 13
Country: Number of subjects enrolled	Germany: 30
Country: Number of subjects enrolled	Italy: 11
Country: Number of subjects enrolled	Netherlands: 18
Country: Number of subjects enrolled	Romania: 34
Country: Number of subjects enrolled	Spain: 19
Country: Number of subjects enrolled	United States: 87
Worldwide total number of subjects	230
EEA total number of subjects	143

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	0

months)	
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	101
From 65 to 84 years	126
85 years and over	3

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

In Part 1, upon determination of PD-L1 status (cut-off of 1%), 2 cohorts were defined: PD-L1 positive and negative. In Part 2, a separate group of participants were treated regardless of their PD-L1 status.

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	PART 1: PD-L1+ Status

Arm description:

Nivolumab + ipilimumab at a flat dose of nivolumab 240 mg as a 30-minute intravenous (IV) infusion every two weeks + ipilimumab 1 mg/kg as a 30-minute IV infusion every 6 weeks. Treatment would continue until disease progression, unacceptable toxicity, withdrawal of consent, the study ending, or a maximum treatment duration of 2 years, whichever occurred first.

Arm type	Experimental
Investigational medicinal product name	Ipilimumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

1 mg/kg 30-minute IV infusion every 6 weeks.

Investigational medicinal product name	Nivolumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

240 mg 30-minute infusion every two weeks.

Arm title	PART 1: PD-L1- Status

Arm description:

Nivolumab + ipilimumab at a flat dose of nivolumab 240 mg as a 30-minute intravenous (IV) infusion every two weeks + ipilimumab 1 mg/kg as a 30-minute IV infusion every 6 weeks. Treatment would continue until disease progression, unacceptable toxicity, withdrawal of consent, the study ending, or a maximum treatment duration of 2 years, whichever occurred first.

Arm type	Experimental
Investigational medicinal product name	Ipilimumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

1 mg/kg 30-minute IV infusion every 6 weeks.

Investigational medicinal product name	Nivolumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

240 mg 30-minute infusion every two weeks.

Arm title	PART 1: Not Evaluable/Indeterminate PD-L1 Status

Arm description:

Nivolumab + ipilimumab at a flat dose of nivolumab 240 mg as a 30-minute intravenous (IV) infusion every two weeks + ipilimumab 1 mg/kg as a 30-minute IV infusion every 6 weeks. Treatment would continue until disease progression, unacceptable toxicity, withdrawal of consent, the study ending, or a maximum treatment duration of 2 years, whichever occurred first.

Arm type	Experimental
Investigational medicinal product name	Ipilimumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

1 mg/kg 30-minute IV infusion every 6 weeks.

Investigational medicinal product name	Nivolumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

240 mg 30-minute infusion every two weeks.

Arm title	PART 2: PD-L1 Status Independent

Arm description:

Nivolumab + ipilimumab at a flat dose of nivolumab 240 mg as a 30-minute intravenous (IV) infusion every two weeks + ipilimumab 1 mg/kg as a 30-minute IV infusion every 6 weeks. Treatment would continue until disease progression, unacceptable toxicity, withdrawal of consent, the study ending, or a maximum treatment duration of 2 years, whichever occurred first

Arm type	Experimental
Investigational medicinal product name	Ipilimumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

1 mg/kg 30-minute IV infusion every 6 weeks.

Investigational medicinal product name	Nivolumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

240 mg 30-minute infusion every two weeks.

Number of subjects in period 1	PART 1: PD-L1+ Status	PART 1: PD-L1- Status	PART 1: Not Evaluable/Indeterminate PD-L1 Status
Started	31	28	1
Completed	0	0	0
Not completed	31	28	1
Adverse event, serious fatal	1	-	-
Disease progression	16	14	1
Participant requested to d/c study treatment	-	-	-
Participant withdrew consent	-	1	-
Not reported	-	-	-
Maximum clinical benefit	2	3	-
AE unrelated to study drug	3	3	-
Other reasons	1	2	-
Study Drug Toxicity	8	5	-
Administrative reason by sponsor	-	-	-

Number of subjects in period 1	PART 2: PD-L1 Status Independent
Started	170
Completed	0
Not completed	170
Adverse event, serious fatal	3
Disease progression	90
Participant requested to d/c study treatment	2
Participant withdrew consent	5
Not reported	6
Maximum clinical benefit	10
AE unrelated to study drug	11
Other reasons	5
Study Drug Toxicity	37
Administrative reason by sponsor	1

Baseline characteristics

Reporting groups	
Reporting group title	PART 1: PD-L1+ Status
Reporting group description:	
Nivolumab + ipilimumab at a flat dose of nivolumab 240 mg as a 30-minute intravenous (IV) infusion every two weeks + ipilimumab 1 mg/kg as a 30-minute IV infusion every 6 weeks. Treatment would continue until disease progression, unacceptable toxicity, withdrawal of consent, the study ending, or a maximum treatment duration of 2 years, whichever occurred first.	
Reporting group title	PART 1: PD-L1- Status
Reporting group description:	
Nivolumab + ipilimumab at a flat dose of nivolumab 240 mg as a 30-minute intravenous (IV) infusion every two weeks + ipilimumab 1 mg/kg as a 30-minute IV infusion every 6 weeks. Treatment would continue until disease progression, unacceptable toxicity, withdrawal of consent, the study ending, or a maximum treatment duration of 2 years, whichever occurred first.	
Reporting group title	PART 1: Not Evaluable/Indeterminate PD-L1 Status
Reporting group description:	
Nivolumab + ipilimumab at a flat dose of nivolumab 240 mg as a 30-minute intravenous (IV) infusion every two weeks + ipilimumab 1 mg/kg as a 30-minute IV infusion every 6 weeks. Treatment would continue until disease progression, unacceptable toxicity, withdrawal of consent, the study ending, or a maximum treatment duration of 2 years, whichever occurred first.	
Reporting group title	PART 2: PD-L1 Status Independent
Reporting group description:	
Nivolumab + ipilimumab at a flat dose of nivolumab 240 mg as a 30-minute intravenous (IV) infusion every two weeks + ipilimumab 1 mg/kg as a 30-minute IV infusion every 6 weeks. Treatment would continue until disease progression, unacceptable toxicity, withdrawal of consent, the study ending, or a maximum treatment duration of 2 years, whichever occurred first	

Reporting group values	PART 1: PD-L1+ Status	PART 1: PD-L1- Status	PART 1: Not Evaluable/Indeterminate PD-L1 Status
Number of subjects	31	28	1
Age Categorical Units: Participants			
<=18 years	0	0	0
Between 18 and 65 years	10	15	0
>=65 years	21	13	1
Sex: Female, Male Units: Participants			
Female	15	11	0
Male	16	17	1
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	1	1	0
Not Hispanic or Latino	24	25	1
Unknown or Not Reported	6	2	0
Race/Ethnicity, Customized			
Race			
Units: Subjects			
White	27	25	1
Black or African American	3	3	0
Other	1	0	0

Reporting group values	PART 2: PD-L1 Status Independent	Total	
Number of subjects	170	230	
Age Categorical Units: Participants			
<=18 years	0	0	
Between 18 and 65 years	76	101	
>=65 years	94	129	
Sex: Female, Male Units: Participants			
Female	54	80	
Male	116	150	
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	4	6	
Not Hispanic or Latino	98	148	
Unknown or Not Reported	68	76	
Race/Ethnicity, Customized			
Race			
Units: Subjects			
White	164	217	
Black or African American	5	11	
Other	1	2	

End points

End points reporting groups

Reporting group title	PART 1: PD-L1+ Status

Reporting group description:

Nivolumab + ipilimumab at a flat dose of nivolumab 240 mg as a 30-minute intravenous (IV) infusion every two weeks + ipilimumab 1 mg/kg as a 30-minute IV infusion every 6 weeks. Treatment would continue until disease progression, unacceptable toxicity, withdrawal of consent, the study ending, or a maximum treatment duration of 2 years, whichever occurred first.

Reporting group title	PART 1: PD-L1- Status

Reporting group description:

Nivolumab + ipilimumab at a flat dose of nivolumab 240 mg as a 30-minute intravenous (IV) infusion every two weeks + ipilimumab 1 mg/kg as a 30-minute IV infusion every 6 weeks. Treatment would continue until disease progression, unacceptable toxicity, withdrawal of consent, the study ending, or a maximum treatment duration of 2 years, whichever occurred first.

Reporting group title	PART 1: Not Evaluable/Indeterminate PD-L1 Status

Reporting group description:

Nivolumab + ipilimumab at a flat dose of nivolumab 240 mg as a 30-minute intravenous (IV) infusion every two weeks + ipilimumab 1 mg/kg as a 30-minute IV infusion every 6 weeks. Treatment would continue until disease progression, unacceptable toxicity, withdrawal of consent, the study ending, or a maximum treatment duration of 2 years, whichever occurred first.

Reporting group title	PART 2: PD-L1 Status Independent

Reporting group description:

Nivolumab + ipilimumab at a flat dose of nivolumab 240 mg as a 30-minute intravenous (IV) infusion every two weeks + ipilimumab 1 mg/kg as a 30-minute IV infusion every 6 weeks. Treatment would continue until disease progression, unacceptable toxicity, withdrawal of consent, the study ending, or a maximum treatment duration of 2 years, whichever occurred first

Subject analysis set title	PART 1: PD-L1 + Status
Subject analysis set type	Per protocol

Subject analysis set description:

Nivolumab + ipilimumab at a flat dose of nivolumab 240 mg as a 30-minute intravenous (IV) infusion every two weeks + ipilimumab 1 mg/kg as a 30-minute IV infusion every 6 weeks. Treatment would continue until disease progression, unacceptable toxicity, withdrawal of consent, the study ending, or a maximum treatment duration of 2 years, whichever occurred first.

Subject analysis set title	PART 2: PD-L1- Status
Subject analysis set type	Per protocol

Subject analysis set description:

Nivolumab + ipilimumab at a flat dose of nivolumab 240 mg as a 30-minute intravenous (IV) infusion every two weeks + ipilimumab 1 mg/kg as a 30-minute IV infusion every 6 weeks. Treatment would continue until disease progression, unacceptable toxicity, withdrawal of consent, the study ending, or a maximum treatment duration of 2 years, whichever occurred first

Subject analysis set title	PART 2: PD-L1 + Status
Subject analysis set type	Per protocol

Subject analysis set description:

Nivolumab + ipilimumab at a flat dose of nivolumab 240 mg as a 30-minute intravenous (IV) infusion every two weeks + ipilimumab 1 mg/kg as a 30-minute IV infusion every 6 weeks. Treatment would continue until disease progression, unacceptable toxicity, withdrawal of consent, the study ending, or a maximum treatment duration of 2 years, whichever occurred first

Subject analysis set title	PART 2: PD-L1 + Status
Subject analysis set type	Per protocol

Subject analysis set description:

Nivolumab + ipilimumab at a flat dose of nivolumab 240 mg as a 30-minute intravenous (IV) infusion every two weeks + ipilimumab 1 mg/kg as a 30-minute IV infusion every 6 weeks. Treatment would continue until disease progression, unacceptable toxicity, withdrawal of consent, the study ending, or a maximum treatment duration of 2 years, whichever occurred first

Subject analysis set title	PART 2: PD-L1- Status
Subject analysis set type	Per protocol

Subject analysis set description:

Nivolumab + ipilimumab at a flat dose of nivolumab 240 mg as a 30-minute intravenous (IV) infusion every two weeks + ipilimumab 1 mg/kg as a 30-minute IV infusion every 6 weeks. Treatment would continue until disease progression, unacceptable toxicity, withdrawal of consent, the study ending, or a maximum treatment duration of 2 years, whichever occurred first

Subject analysis set title	PART 1
Subject analysis set type	Per protocol

Subject analysis set description:

Nivolumab + ipilimumab at a flat dose of nivolumab 240 mg as a 30-minute intravenous (IV) infusion every two weeks + ipilimumab 1 mg/kg as a 30-minute IV infusion every 6 weeks. Treatment would continue until disease progression, unacceptable toxicity, withdrawal of consent, the study ending, or a maximum treatment duration of 2 years, whichever occurred first.

Subject analysis set title	PART 2
Subject analysis set type	Per protocol

Subject analysis set description:

Nivolumab + ipilimumab at a flat dose of nivolumab 240 mg as a 30-minute intravenous (IV) infusion every two weeks + ipilimumab 1 mg/kg as a 30-minute IV infusion every 6 weeks. Treatment would continue until disease progression, unacceptable toxicity, withdrawal of consent, the study ending, or a maximum treatment duration of 2 years, whichever occurred first

Subject analysis set title	PART 1
Subject analysis set type	Per protocol

Subject analysis set description:

Nivolumab + ipilimumab at a flat dose of nivolumab 240 mg as a 30-minute intravenous (IV) infusion every two weeks + ipilimumab 1 mg/kg as a 30-minute IV infusion every 6 weeks. Treatment would continue until disease progression, unacceptable toxicity, withdrawal of consent, the study ending, or a maximum treatment duration of 2 years, whichever occurred first.

Subject analysis set title	PART 2
Subject analysis set type	Per protocol

Subject analysis set description:

Nivolumab + ipilimumab at a flat dose of nivolumab 240 mg as a 30-minute intravenous (IV) infusion every two weeks + ipilimumab 1 mg/kg as a 30-minute IV infusion every 6 weeks. Treatment would continue until disease progression, unacceptable toxicity, withdrawal of consent, the study ending, or a maximum treatment duration of 2 years, whichever occurred first

Primary: Objective Response Rate (ORR) per Investigator by Blood TMB (bTMB) within PD-L1 Subgroup (TMB Cut-point = 16 mutations/MB)

End point title	Objective Response Rate (ORR) per Investigator by Blood TMB (bTMB) within PD-L1 Subgroup (TMB Cut-point = 16 mutations/MB)[1][2]

End point description:

Objective response rate (ORR) is defined as the percent of treated participants with a best overall response of a complete response (CR) or partial response (PR) assessed by investigator per Response Evaluation Criteria In Solid Tumors (RECIST 1.1).
PR is at least a 30% decrease in the sum of diameters of target lesions, taking as reference the baseline sum diameters. CR is disappearance of all target lesions and a reduction in pathological lymph node (whether target or non-target) short axis to <10 mm.
Blood tumor mutational burden (bTMB) is the total number of nonsynonymous somatic mutations produced by a tumor that are detected in serum.
CR+PR, confidence interval based on the Clopper and Pearson method.

End point type	Primary

End point timeframe:

From first dose up to the date of objectively documented progression, or the date of initiation of palliative local therapy or the date of initiation of subsequent anticancer therapy (up to approximately 58 months)

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only summary analysis planned for this endpoint.

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the

baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only summary analysis planned for pre-specified arms.

End point values	PART 1: PD-L1- Status	PART 1: Not Evaluable/Indeterminate PD-L1 Status	PART 1: PD-L1 + Status	PART 2: PD-L1- Status
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	16	0[3]	19	62
Units: Percent of Participants				
number (confidence interval 95%)				
bTMB High (Cut-point = 16-mutations)	50 (18.7 to 81.3)	(to)	30 (6.7 to 65.2)	30.3 (15.6 to 48.7)
bTMB Low (Cut-point = 16-mutations)	33.3 (4.3 to 77.7)	(to)	33.3 (7.5 to 70.1)	24.1 (10.3 to 43.5)

Notes:
[3] - 0 participants analyzed

End point values	PART 2: PD-L1 + Status			
Subject group type	Subject analysis set			
Number of subjects analysed	39			
Units: Percent of Participants				
number (confidence interval 95%)				
bTMB High (Cut-point = 16-mutations)	58.8 (32.9 to 81.6)			
bTMB Low (Cut-point = 16-mutations)	31.8 (13.9 to 54.9)			

Statistical analyses

No statistical analyses for this end point

Primary: Objective Response Rate (ORR) per Investigator by Blood TMB (bTMB) within PD-L1 Subgroup (Blood TMB Cut-point = 21-mutations/MB)

End point title	Objective Response Rate (ORR) per Investigator by Blood TMB (bTMB) within PD-L1 Subgroup (Blood TMB Cut-point = 21-mutations/MB)[4][5]

End point description:

Objective response rate (ORR) is defined as the percent of treated participants with a best overall response of a complete response (CR) or partial response (PR) assessed by investigator per Response Evaluation Criteria In Solid Tumors (RECIST 1.1).
PR is at least a 30% decrease in the sum of diameters of target lesions, taking as reference the baseline sum diameters. CR is disappearance of all target lesions and a reduction in pathological lymph node (whether target or non-target) short axis to <10 mm.
Blood tumor mutational burden (bTMB) is the total number of nonsynonymous somatic mutations produced by a tumor that are detected in serum.
CR+PR, confidence interval based on the Clopper and Pearson method.

End point type	Primary

End point timeframe:

From first dose up to the date of objectively documented progression, or the date of initiation of palliative local therapy or the date of initiation of subsequent anticancer therapy (up to approximately 58 months)

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only summary analysis planned for this endpoint.

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only summary analysis planned for pre-specified arms.

End point values	PART 1: PD-L1+ Status	PART 1: PD-L1- Status	PART 1: Not Evaluable/Indeterminate PD-L1 Status	PART 2: PD-L1- Status
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	19	16	0[6]	62
Units: Percent of Participants				
number (confidence interval 95%)				
bTMB High (Cut-point = 21-mutations)	33.3 (4.3 to 77.7)	66.7 (22.3 to 95.7)	(to)	40.9 (20.7 to 63.6)
bTMB Low (Cut-point = 21-mutations)	30.8 (9.1 to 61.4)	30.0 (6.7 to 65.2)	(to)	20.0 (9.1 to 35.6)

Notes:

[6] - 0 participants analyzed

End point values	PART 2: PD-L1+ Status			
Subject group type	Subject analysis set			
Number of subjects analysed	39			
Units: Percent of Participants				
number (confidence interval 95%)				
bTMB High (Cut-point = 21-mutations)	64.3 (35.1 to 87.2)			
bTMB Low (Cut-point = 21-mutations)	32.0 (14.9 to 53.5)			

Statistical analyses

No statistical analyses for this end point

Primary: Objective Response Rate (ORR) per Investigator by Tissue TMB within PD-L1 Subgroup (Tissue TMB Cut-point = 10-mutations/MB)

End point title	Objective Response Rate (ORR) per Investigator by Tissue TMB within PD-L1 Subgroup (Tissue TMB Cut-point = 10-mutations/MB)[7][8]

End point description:

Objective response rate (ORR) is defined as the percent of treated participants with a best overall response of a complete response (CR) or partial response (PR) assessed by investigator per Response Evaluation Criteria In Solid Tumors (RECIST 1.1).
PR is at least a 30% decrease in the sum of diameters of target lesions, taking as reference the baseline sum diameters. CR is disappearance of all target lesions and a reduction in pathological lymph node (whether target or non-target) short axis to <10 mm.
Tissue tumor mutational burden (tTMB) is the total number of nonsynonymous somatic mutations produced by a tumor that are detected in tumor tissue samples.
CR+PR, confidence interval based on the Clopper and Pearson method.

End point type	Primary

End point timeframe:

From first dose up to the date of objectively documented progression, or the date of initiation of palliative local therapy or the date of initiation of subsequent anticancer therapy (up to approximately 58 months)

Notes:

[7] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only summary analysis planned for this endpoint.

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only summary analysis planned for pre-specified arms.

End point values	PART 1: PD-L1+ Status	PART 1: PD-L1- Status	PART 1: Not Evaluable/Indeterminate PD-L1 Status	PART 2: PD-L1 + Status
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	19	16	0[9]	31
Units: Percent of Participants				
number (confidence interval 95%)				
tTMB High (Cut-point = 10-mutations)	25.0 (3.2 to 65.1)	71.4 (29.0 to 96.3)	(to)	60.0 (32.3 to 83.7)
tTMB Low (Cut-point = 10-mutations	27.3 (6.0 to 61.0)	22.2 (2.8 to 60.0)	(to)	25.0 (7.3 to 52.4)

Notes:

[9] - 0 participants analyzed

End point values	PART 2: PD-L1- Status			
Subject group type	Subject analysis set			
Number of subjects analysed	57			
Units: Percent of Participants				
number (confidence interval 95%)				
tTMB High (Cut-point = 10-mutations)	46.7 (21.3 to 73.4)			
tTMB Low (Cut-point = 10-mutations	21.4 (10.3 to 36.8)			

Statistical analyses

No statistical analyses for this end point

Secondary: Objective Response Rate (ORR) for All Treated Participants by Investigator per RECIST 1.1

End point title	Objective Response Rate (ORR) for All Treated Participants by Investigator per RECIST 1.1

End point description:

Objective response rate (ORR) is defined as the percent of treated participants with a best overall response of a complete response (CR) or partial response (PR) assessed by investigator per Response Evaluation Criteria In Solid Tumors (RECIST 1.1).
Partial Response (PR) is at least a 30% decrease in the sum of diameters of target lesions, taking as reference the baseline sum diameters. Complete Response (CR) is disappearance of all target lesions and a reduction in pathological lymph node (whether target or non-target) short axis to <10 mm.
CR+PR, confidence interval based on the Clopper and Pearson method.

End point type	Secondary

End point timeframe:

From first dose until the date of objectively documented progression, or the date of initiation of palliative local therapy or the date of initiation of subsequent anticancer therapy, whichever occurs first (Up to approximately 67 months)

End point values	PART 1: PD-L1+ Status	PART 1: PD-L1- Status	PART 1: Not Evaluable/Indeterminate PD-L1 Status	PART 2: PD-L1 Status Independent
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	31	28	1	170
Units: Percent of Participants				
number (confidence interval 95%)	29.0 (14.2 to 48.0)	39.3 (21.5 to 59.4)	0 (0.0 to 97.5)	29.4 (22.7 to 36.9)

Statistical analyses

No statistical analyses for this end point

Secondary: Disease Control Rate (DCR) for Part 1

End point title	Disease Control Rate (DCR) for Part 1[10]

End point description:

Disease control rate (DCR) is the percent of treated participants with a best overall response of a complete response (CR), partial response (PR), or stable disease (SD), assessed by investigator per Response Evaluation Criteria In Solid Tumors (RECIST 1.1).
PR is at least a 30% decrease in the sum of diameters of target lesions, using the baseline sum diameters as reference. CR is disappearance of all target lesions and a reduction in short axis to <10 mm of any pathological lymph nodes (target or non-target). SD is neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for progressive disease (PD), taking smallest sum diameters as reference. PD is at least a 20% increase in the sum of diameters of target lesions, taking the smallest sum as reference. The sum must also demonstrate an absolute increase of at least 5 mm. (one or more new lesions is also considered progression). CR+PR, confidence interval based on the Clopper and Pearson method.

End point type	Secondary

End point timeframe:

From first dose until the date of objectively documented progression, or the date of initiation of palliative local therapy or the date of initiation of subsequent anticancer therapy, whichever occurs first (Up to approximately 67 months)

Notes:

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only summary analysis planned for pre-specified arms.

End point values	PART 1: PD-L1+ Status	PART 1: PD-L1- Status	PART 1: Not Evaluable/Indeterminate PD-L1 Status	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	31	28	1	
Units: Percent of Participants				
number (confidence interval 95%)	58.1 (39.1 to 75.5)	64.3 (44.1 to 81.4)	100.0 (2.5 to 100.0)	

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (DOR) for Part 1

End point title	Duration of Response (DOR) for Part 1[11]

End point description:

DOR is the time between first confirmed response (Complete/Partial Response) and first documented tumor progression (per RECIST 1.1) or death due to any cause. Participants who don't progress or die are censored on the date of their last evaluable tumor assessment. Participants who started subsequent anti-cancer therapy without prior reported progression were censored at the last evaluable tumor assessment prior to or on the date of subsequent anti-cancer therapy.
PR is at least 30% decrease in the sum of diameters of target lesions, using baseline sum diameters as reference. CR is disappearance of all target lesions and reduction in short axis to <10 mm of any pathological lymph nodes (target or non-target). Progressive Disease (PD) is at least 20% increase in the sum of diameters of target lesions, taking the smallest sum as reference. The sum must also show an overall increase of > 5 mm. (one or more new lesions is also progression). Median computed using Kaplan-Meier method.

End point type	Secondary

End point timeframe:

From first dose to the date of the first documented tumor progression or death due to any cause (Up to approximately 67 months)

Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only summary analysis planned for pre-specified arms.

End point values	PART 1: PD-L1+ Status	PART 1: PD-L1- Status	PART 1: Not Evaluable/Indeterminate PD-L1 Status	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	9	11	0[12]	
Units: Months				
median (full range (min-max))	24.56 (1.9 to 61.7)	29.57 (2.8 to 48.9)	(to)	

Notes:

[12] - 0 participants analyzed

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Response (TTR) for Part 1

End point title	Time to Response (TTR) for Part 1[13]

End point description:

TTR is the time taken from first dosing date to the time the criteria for Complete Response (CR)/Partial Response (PR) are first met.
Partial Response (PR) is at least a 30% decrease in the sum of diameters of target lesions, taking as

reference the baseline sum diameters. Complete Response (CR) is disappearance of all target lesions. Any pathological lymph nodes (whether target or non-target) must have reduction in short axis to <10 mm.

End point type	Secondary

End point timeframe:

From first dose to the time the criteria for Complete Response/Partial Response are first met (Up to approximately 67 months)

Notes:

[13] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only summary analysis planned for pre-specified arms.

End point values	PART 1: PD-L1+ Status	PART 1: PD-L1- Status	PART 1: Not Evaluable/Indeterminate PD-L1 Status	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	9	11	0[14]	
Units: Months				
median (full range (min-max))	1.84 (1.6 to 3.7)	5.26 (1.7 to 18.5)	(to)	

Notes:

[14] - 0 participants analyzed

Statistical analyses

No statistical analyses for this end point

Secondary: Progression Free Survival (PFS)

End point title	Progression Free Survival (PFS)

End point description:

PFS is defined as the time from first dosing date to the date of the first documented tumor progression (per RECIST 1.1) or death due to any cause.
Participants who neither progress nor die will be censored on the date of their last evaluable tumor assessment. Participants who started any subsequent anti-cancer therapy without a prior reported progression will be censored at the last evaluable tumor assessment prior to or on the date of initiation of subsequent anti-cancer therapy.
Progressive Disease (PD) is at least a 20% increase in the sum of diameters of target lesions, taking the smallest sum on study as reference. The sum must also show an overall increase of > 5 mm. (one or more new lesions is also progression).
Median calculated using Kaplan-Meier estimates.
+/-99999=NA

End point type	Secondary

End point timeframe:

From first dose to the date of the first documented tumor progression or death due to any causes (Assessed up to approximately 67 months)

End point values	PART 1: PD-L1+ Status	PART 1: PD-L1- Status	PART 1: Not Evaluable/Indeterminate PD-L1 Status	PART 2: PD-L1 Status Independent
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	31	28	1	170
Units: Months				
median (confidence interval 95%)	3.71 (1.97 to 8.90)	4.30 (1.84 to 13.60)	3.61 (-99999 to 99999)	6.28 (5.09 to 7.56)

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS)

End point title	Overall Survival (OS)

End point description:

OS is defined as the time from first dosing date to the date of death. If a participant didn't die, OS will be censored on the last date the participant was known to be alive.
Median based on Kaplan-Meier estimates.
+/-99999=NA

End point type	Secondary

End point timeframe:

From first dose to the date of death (Assessed up to approximately 67 months)

End point values	PART 1: PD-L1+ Status	PART 1: PD-L1- Status	PART 1: Not Evaluable/Indeterminate PD-L1 Status	PART 2: PD-L1 Status Independent
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	31	28	1	170
Units: Months				
median (confidence interval 95%)	9.63 (4.47 to 20.57)	22.29 (11.56 to 25.23)	9.23 (-99999 to 99999)	14.78 (11.99 to 20.60)

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Adverse Events (AEs) for Study Part 2

End point title	Number of Participants with Adverse Events (AEs) for Study Part 2[15]

End point description:

An Adverse Event (AE) is any new untoward medical occurrence or worsening preexisting medical condition in a treated participant and that does not necessarily have a causal relationship with treatment.
An AE can be any unfavorable, unintended sign, symptom, or disease temporally associated with the use of treatment, whether or not related to the treatment.

End point type	Secondary

End point timeframe:

From first dose to 30 days after last dosing date (assessed up to approximately 27 months)

Notes:

[15] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only summary analysis planned for pre-specified arms.

End point values	PART 2: PD-L1 Status Independent			
Subject group type	Reporting group			
Number of subjects analysed	170			
Units: Participants	169			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Serious Adverse Events (SAEs) for Study Part 2

End point title	Number of Participants with Serious Adverse Events (SAEs) for Study Part 2[16]

End point description:

A Serious Adverse Event (SAE) results in death, is life-threatening (defined as an event in which the participant was at risk of death at the time of the event; it does not refer to an event which hypothetically might have caused death if it were more severe), or requires inpatient hospitalization or causes prolongation of existing hospitalization.

End point type	Secondary

End point timeframe:

From first dose to 30 days after last dosing date (assessed up to approximately 27 months)

Notes:

[16] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only summary analysis planned for pre-specified arms.

End point values	PART 2: PD-L1 Status Independent			
Subject group type	Reporting group			
Number of subjects analysed	170			
Units: Participants	102			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Select Adverse Events (AEs) for Study Part 2

End point title	Number of Participants with Select Adverse Events (AEs) for Study Part 2[17]

End point description:

An Adverse Event (AE) is any new untoward medical occurrence or worsening preexisting medical condition in a treated participant and that does not necessarily have a causal relationship with treatment.
An AE can be any unfavorable, unintended sign, symptom, or disease temporally associated with the use of treatment, whether or not related to the treatment.

End point type	Secondary

End point timeframe:

From first dose to 30 days after last dosing date (up to approximately 27 months)

Notes:

[17] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only summary analysis planned for pre-specified arms.

End point values	PART 2: PD-L1 Status Independent			
Subject group type	Reporting group			
Number of subjects analysed	170			
Units: Participants				
Gastrointestinal Adverse Events	68			
Hepatic Adverse Events	49			
Pulmonary Adverse Events	17			
Renal Adverse Events	28			
Skin Adverse Events	73			
Hypersensitivity/Infusion Reaction	12			

Statistical analyses

No statistical analyses for this end point

Post-hoc: Extended Collection of Objective Response Rate (ORR) per Investigator by Blood TMB (bTMB) (TMB Cut-point = 16 mutations/MB)

End point title	Extended Collection of Objective Response Rate (ORR) per Investigator by Blood TMB (bTMB) (TMB Cut-point = 16 mutations/MB)[18]

End point description:

Objective response rate (ORR) is defined as the percent of treated participants with a best overall response of a complete response (CR) or partial response (PR) assessed by investigator per Response Evaluation Criteria In Solid Tumors (RECIST 1.1).
PR is at least a 30% decrease in the sum of diameters of target lesions, taking as reference the baseline sum diameters. CR is disappearance of all target lesions and a reduction in pathological lymph node (whether target or non-target) short axis to <10 mm.
Blood tumor mutational burden (bTMB) is the total number of nonsynonymous somatic mutations produced by a tumor that are detected in serum.
CR+PR, confidence interval based on the Clopper and Pearson method.

End point type	Post-hoc

End point timeframe:

From first dose up to the date of objectively documented progression, or the date of initiation of palliative local therapy or the date of initiation of subsequent anticancer therapy (up to approximately 67 months)

Notes:

[18] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only summary analysis planned for pre-specified arms.

End point values	PART 1: Not Evaluable/Indeterminate PD-L1 Status	PART 1	PART 2	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	0[19]	36	131	
Units: Percent of Participants				
number (confidence interval 95%)				
bTMB High (Cut-point = 16-mutations)	(to)	40.0 (19.1 to 63.9)	34.3 (22.9 to 47.3)	
bTMB Low (Cut-point = 16-mutations)	(to)	25.0 (7.3 to 52.4)	26.9 (16.8 to 39.1)	

Notes:

[19] - 0 participants analyzed

Statistical analyses

No statistical analyses for this end point

Post-hoc: Extended Collection of Objective Response Rate (ORR) per Investigator by Blood TMB (bTMB) (Blood TMB Cut-point = 21-mutations/MB)

End point title	Extended Collection of Objective Response Rate (ORR) per Investigator by Blood TMB (bTMB) (Blood TMB Cut-point = 21-mutations/MB)[20]

End point description:

Objective response rate (ORR) is defined as the percent of treated participants with a best overall response of a complete response (CR) or partial response (PR) assessed by investigator per Response Evaluation Criteria In Solid Tumors (RECIST 1.1).
PR is at least a 30% decrease in the sum of diameters of target lesions, taking as reference the baseline sum diameters. CR is disappearance of all target lesions and a reduction in pathological lymph node (whether target or non-target) short axis to <10 mm.
Blood tumor mutational burden (bTMB) is the total number of nonsynonymous somatic mutations produced by a tumor that are detected in serum.
CR+PR, confidence interval based on the Clopper and Pearson method.

End point type	Post-hoc

End point timeframe:

From first dose up to the date of objectively documented progression, or the date of initiation of palliative local therapy or the date of initiation of subsequent anticancer therapy (up to approximately 67 months)

Notes:

[20] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only summary analysis planned for pre-specified arms.

End point values	PART 1: Not Evaluable/Indeterminate PD-L1 Status	PART 1	PART 2	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	0[21]	36	131	
Units: Percent of Participants				

number (confidence interval 95%)				
bTMB High (Cut-point = 21-mutations)	(to)	50.0 (21.1 to 78.9)	44.4 (29.6 to 60.0)	
bTMB Low (Cut-point = 21-mutations)	(to)	25.0 (9.8 to 46.7)	23.3 (14.8 to 33.6)	

Notes:

[21] - 0 participants analyzed

Statistical analyses

No statistical analyses for this end point

Post-hoc: Extended Collection of Objective Response Rate (ORR) per Investigator by Tissue TMB (Tissue TMB Cut-point = 10-mutations/MB)

End point title	Extended Collection of Objective Response Rate (ORR) per Investigator by Tissue TMB (Tissue TMB Cut-point = 10-mutations/MB)[22]

End point description:

Objective response rate (ORR) is defined as the percent of treated participants with a best overall response of a complete response (CR) or partial response (PR) assessed by investigator per Response Evaluation Criteria In Solid Tumors (RECIST 1.1).
PR is at least a 30% decrease in the sum of diameters of target lesions, taking as reference the baseline sum diameters. CR is disappearance of all target lesions and a reduction in pathological lymph node (whether target or non-target) short axis to <10 mm.
Tissue tumor mutational burden (tTMB) is the total number of nonsynonymous somatic mutations produced by a tumor that are detected in tumor tissue samples.
CR+PR, confidence interval based on the Clopper and Pearson method.

End point type	Post-hoc

End point timeframe:

From first dose up to the date of objectively documented progression, or the date of initiation of palliative local therapy or the date of initiation of subsequent anticancer therapy (up to approximately 67 months)

Notes:

[22] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only summary analysis planned for pre-specified arms.

End point values	PART 1: Not Evaluable/Indeterminate PD-L1 Status	PART 1	PART 2	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	0[23]	35	101	
Units: Percent of Participants				
number (confidence interval 95%)				
tTMB High (Cut-point = 10-mutations)	(to)	46.7 (21.3 to 73.4)	50.0 (32.4 to 67.6)	
tTMB Low (Cut-point = 10-mutations	(to)	20.0 (5.7 to 43.7)	19.4 (10.8 to 30.9)	

Notes:

[23] - 0 participants analyzed

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Subjects assessed for Deaths (all-causes) from their first dose to their study completion (up to 67 months.) SAEs and NSAEs were assessed from first dose to 100 days post last dose (up to an avg. of 8 months and a max. of 29 months).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	26.0

Reporting groups

Reporting group title	PART 1: PD-L1+ Status

Reporting group description:

Nivolumab + ipilimumab at a flat dose of nivolumab 240 mg as a 30-minute intravenous (IV) infusion every two weeks + ipilimumab 1 mg/kg as a 30-minute IV infusion every 6 weeks. Treatment would continue until disease progression, unacceptable toxicity, withdrawal of consent, the study ending, or a maximum treatment duration of 2 years, whichever occurred first.

Reporting group title	PART 2: PD-L1 Status Independent

Reporting group description:

Nivolumab + ipilimumab at a flat dose of nivolumab 240 mg as a 30-minute intravenous (IV) infusion every two weeks + ipilimumab 1 mg/kg as a 30-minute IV infusion every 6 weeks. Treatment would continue until disease progression, unacceptable toxicity, withdrawal of consent, the study ending, or a maximum treatment duration of 2 years, whichever occurred first

Reporting group title	PART 1: Not Evaluable/Indeterminate PD-L1 Status

Reporting group description:

Nivolumab + ipilimumab at a flat dose of nivolumab 240 mg as a 30-minute intravenous (IV) infusion every two weeks + ipilimumab 1 mg/kg as a 30-minute IV infusion every 6 weeks. Treatment would continue until disease progression, unacceptable toxicity, withdrawal of consent, the study ending, or a maximum treatment duration of 2 years, whichever occurred first.

Reporting group title	PART 1: PD-L1- Status

Reporting group description:

Nivolumab + ipilimumab at a flat dose of nivolumab 240 mg as a 30-minute intravenous (IV) infusion every two weeks + ipilimumab 1 mg/kg as a 30-minute IV infusion every 6 weeks. Treatment would continue until disease progression, unacceptable toxicity, withdrawal of consent, the study ending, or a maximum treatment duration of 2 years, whichever occurred first.

Serious adverse events	PART 1: PD-L1+ Status	PART 2: PD-L1 Status Independent	PART 1: Not Evaluable/Indeterminate PD-L1 Status
Total subjects affected by serious adverse events			
subjects affected / exposed	24 / 31 (77.42%)	113 / 170 (66.47%)	0 / 1 (0.00%)
number of deaths (all causes)	27	134	1
number of deaths resulting from adverse events	15	49	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignant neoplasm progression			

subjects affected / exposed	10 / 31 (32.26%)	38 / 170 (22.35%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 10	0 / 40	0 / 0
deaths causally related to treatment / all	0 / 10	0 / 36	0 / 0
Cancer pain			
subjects affected / exposed	0 / 31 (0.00%)	2 / 170 (1.18%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malignant pleural effusion			
subjects affected / exposed	0 / 31 (0.00%)	1 / 170 (0.59%)	0 / 1 (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
Phaeochromocytoma			
subjects affected / exposed	0 / 31 (0.00%)	1 / 170 (0.59%)	0 / 1 (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
Non-small cell lung cancer			
subjects affected / exposed	0 / 31 (0.00%)	1 / 170 (0.59%)	0 / 1 (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
Neoplasm progression			
subjects affected / exposed	0 / 31 (0.00%)	1 / 170 (0.59%)	0 / 1 (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
Metastases to central nervous system			
subjects affected / exposed	0 / 31 (0.00%)	1 / 170 (0.59%)	0 / 1 (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
Tumour associated fever			
subjects affected / exposed	0 / 31 (0.00%)	1 / 170 (0.59%)	0 / 1 (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
Tumour ulceration			

subjects affected / exposed	0 / 31 (0.00%)	0 / 170 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tumour necrosis			
subjects affected / exposed	0 / 31 (0.00%)	1 / 170 (0.59%)	0 / 1 (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
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 31 (0.00%)	3 / 170 (1.76%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Embolism			
subjects affected / exposed	0 / 31 (0.00%)	1 / 170 (0.59%)	0 / 1 (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
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	0 / 31 (0.00%)	1 / 170 (0.59%)	0 / 1 (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
Asthenia			
subjects affected / exposed	1 / 31 (3.23%)	0 / 170 (0.00%)	0 / 1 (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
Chest pain			
subjects affected / exposed	0 / 31 (0.00%)	2 / 170 (1.18%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Death			
subjects affected / exposed	1 / 31 (3.23%)	0 / 170 (0.00%)	0 / 1 (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

Adverse drug reaction			
subjects affected / exposed	0 / 31 (0.00%)	1 / 170 (0.59%)	0 / 1 (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
General physical health deterioration			
subjects affected / exposed	0 / 31 (0.00%)	4 / 170 (2.35%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Inflammation			
subjects affected / exposed	0 / 31 (0.00%)	2 / 170 (1.18%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Non-cardiac chest pain			
subjects affected / exposed	0 / 31 (0.00%)	1 / 170 (0.59%)	0 / 1 (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
Systemic inflammatory response syndrome			
subjects affected / exposed	0 / 31 (0.00%)	1 / 170 (0.59%)	0 / 1 (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
Performance status decreased			
subjects affected / exposed	0 / 31 (0.00%)	1 / 170 (0.59%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	0 / 31 (0.00%)	5 / 170 (2.94%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	3 / 6	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Sudden death			
subjects affected / exposed	0 / 31 (0.00%)	3 / 170 (1.76%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 3	0 / 0
Pain			

subjects affected / exposed	0 / 31 (0.00%)	3 / 170 (1.76%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 31 (0.00%)	1 / 170 (0.59%)	0 / 1 (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
Reproductive system and breast disorders			
Adnexa uteri mass			
subjects affected / exposed	0 / 31 (0.00%)	0 / 170 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	2 / 31 (6.45%)	1 / 170 (0.59%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Chronic obstructive pulmonary disease			
subjects affected / exposed	1 / 31 (3.23%)	3 / 170 (1.76%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	0 / 31 (0.00%)	10 / 170 (5.88%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 10	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epistaxis			
subjects affected / exposed	0 / 31 (0.00%)	1 / 170 (0.59%)	0 / 1 (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
Pulmonary embolism			

subjects affected / exposed	1 / 31 (3.23%)	3 / 170 (1.76%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 3	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Hypoxia			
subjects affected / exposed	0 / 31 (0.00%)	2 / 170 (1.18%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Immune-mediated lung disease			
subjects affected / exposed	0 / 31 (0.00%)	1 / 170 (0.59%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Pleural effusion			
subjects affected / exposed	0 / 31 (0.00%)	6 / 170 (3.53%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 6	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Pneumonitis			
subjects affected / exposed	3 / 31 (9.68%)	7 / 170 (4.12%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	3 / 3	9 / 9	0 / 0
deaths causally related to treatment / all	1 / 1	1 / 1	0 / 0
Pulmonary haemorrhage			
subjects affected / exposed	1 / 31 (3.23%)	0 / 170 (0.00%)	0 / 1 (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
Pulmonary oedema			
subjects affected / exposed	0 / 31 (0.00%)	1 / 170 (0.59%)	0 / 1 (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
Respiratory distress			
subjects affected / exposed	0 / 31 (0.00%)	1 / 170 (0.59%)	0 / 1 (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
Respiratory failure			

subjects affected / exposed	1 / 31 (3.23%)	2 / 170 (1.18%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Psychiatric disorders			
Confusional state			
subjects affected / exposed	0 / 31 (0.00%)	2 / 170 (1.18%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	2 / 31 (6.45%)	2 / 170 (1.18%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	2 / 2	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Amylase increased			
subjects affected / exposed	3 / 31 (9.68%)	0 / 170 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	2 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 31 (3.23%)	1 / 170 (0.59%)	0 / 1 (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
Blood bilirubin increased			
subjects affected / exposed	0 / 31 (0.00%)	1 / 170 (0.59%)	0 / 1 (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
General physical condition abnormal			
subjects affected / exposed	0 / 31 (0.00%)	1 / 170 (0.59%)	0 / 1 (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
Lipase increased			
subjects affected / exposed	2 / 31 (6.45%)	1 / 170 (0.59%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	2 / 2	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Troponin I increased			
subjects affected / exposed	0 / 31 (0.00%)	0 / 170 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood creatinine increased			
subjects affected / exposed	1 / 31 (3.23%)	2 / 170 (1.18%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Compression fracture			
subjects affected / exposed	0 / 31 (0.00%)	1 / 170 (0.59%)	0 / 1 (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
Brachial plexus injury			
subjects affected / exposed	1 / 31 (3.23%)	0 / 170 (0.00%)	0 / 1 (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
Depressed fracture			
subjects affected / exposed	0 / 31 (0.00%)	1 / 170 (0.59%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fall			
subjects affected / exposed	1 / 31 (3.23%)	1 / 170 (0.59%)	0 / 1 (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
Hip fracture			
subjects affected / exposed	0 / 31 (0.00%)	0 / 170 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infusion related reaction			
subjects affected / exposed	0 / 31 (0.00%)	1 / 170 (0.59%)	0 / 1 (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

Tendon rupture			
subjects affected / exposed	0 / 31 (0.00%)	1 / 170 (0.59%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 31 (0.00%)	1 / 170 (0.59%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial flutter			
subjects affected / exposed	1 / 31 (3.23%)	0 / 170 (0.00%)	0 / 1 (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
Cardiac arrest			
subjects affected / exposed	0 / 31 (0.00%)	1 / 170 (0.59%)	0 / 1 (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
Cardiac tamponade			
subjects affected / exposed	1 / 31 (3.23%)	1 / 170 (0.59%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Tachycardia			
subjects affected / exposed	0 / 31 (0.00%)	1 / 170 (0.59%)	0 / 1 (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
Nodal rhythm			
subjects affected / exposed	0 / 31 (0.00%)	1 / 170 (0.59%)	0 / 1 (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
Pericardial effusion			
subjects affected / exposed	0 / 31 (0.00%)	5 / 170 (2.94%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 5	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinus tachycardia			

subjects affected / exposed	0 / 31 (0.00%)	0 / 170 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardio-respiratory arrest			
subjects affected / exposed	0 / 31 (0.00%)	1 / 170 (0.59%)	0 / 1 (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
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 31 (0.00%)	0 / 170 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrovascular accident			
subjects affected / exposed	1 / 31 (3.23%)	1 / 170 (0.59%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Hemiparesis			
subjects affected / exposed	0 / 31 (0.00%)	1 / 170 (0.59%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Headache			
subjects affected / exposed	0 / 31 (0.00%)	1 / 170 (0.59%)	0 / 1 (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
Encephalitis autoimmune			
subjects affected / exposed	1 / 31 (3.23%)	0 / 170 (0.00%)	0 / 1 (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
Ischaemic stroke			
subjects affected / exposed	0 / 31 (0.00%)	1 / 170 (0.59%)	0 / 1 (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
Radiculopathy			

subjects affected / exposed	0 / 31 (0.00%)	1 / 170 (0.59%)	0 / 1 (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
Metabolic encephalopathy			
subjects affected / exposed	2 / 31 (6.45%)	0 / 170 (0.00%)	0 / 1 (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
Neuralgia			
subjects affected / exposed	0 / 31 (0.00%)	1 / 170 (0.59%)	0 / 1 (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
Polyneuropathy			
subjects affected / exposed	0 / 31 (0.00%)	1 / 170 (0.59%)	0 / 1 (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
Lethargy			
subjects affected / exposed	1 / 31 (3.23%)	0 / 170 (0.00%)	0 / 1 (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
Syncope			
subjects affected / exposed	0 / 31 (0.00%)	1 / 170 (0.59%)	0 / 1 (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
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 31 (0.00%)	1 / 170 (0.59%)	0 / 1 (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
Thrombocytopenia			
subjects affected / exposed	0 / 31 (0.00%)	1 / 170 (0.59%)	0 / 1 (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
Gastrointestinal disorders			

Abdominal pain			
subjects affected / exposed	0 / 31 (0.00%)	1 / 170 (0.59%)	0 / 1 (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
Diarrhoea			
subjects affected / exposed	0 / 31 (0.00%)	9 / 170 (5.29%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	6 / 9	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Ascites			
subjects affected / exposed	0 / 31 (0.00%)	1 / 170 (0.59%)	0 / 1 (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
Autoimmune pancreatitis			
subjects affected / exposed	1 / 31 (3.23%)	0 / 170 (0.00%)	0 / 1 (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
Constipation			
subjects affected / exposed	0 / 31 (0.00%)	1 / 170 (0.59%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anal fissure			
subjects affected / exposed	1 / 31 (3.23%)	0 / 170 (0.00%)	0 / 1 (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
Dysphagia			
subjects affected / exposed	1 / 31 (3.23%)	0 / 170 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enterocolitis			
subjects affected / exposed	0 / 31 (0.00%)	0 / 170 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric haemorrhage			

subjects affected / exposed	0 / 31 (0.00%)	0 / 170 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	0 / 31 (0.00%)	1 / 170 (0.59%)	0 / 1 (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
Immune-mediated enterocolitis			
subjects affected / exposed	0 / 31 (0.00%)	1 / 170 (0.59%)	0 / 1 (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
Intestinal obstruction			
subjects affected / exposed	0 / 31 (0.00%)	1 / 170 (0.59%)	0 / 1 (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
Intestinal perforation			
subjects affected / exposed	0 / 31 (0.00%)	1 / 170 (0.59%)	0 / 1 (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
Gastritis			
subjects affected / exposed	0 / 31 (0.00%)	2 / 170 (1.18%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis			
subjects affected / exposed	0 / 31 (0.00%)	2 / 170 (1.18%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal haemorrhage			
subjects affected / exposed	0 / 31 (0.00%)	1 / 170 (0.59%)	0 / 1 (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
Vomiting			

subjects affected / exposed	1 / 31 (3.23%)	2 / 170 (1.18%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	2 / 5	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Hepatobiliary disorders			
Autoimmune hepatitis			
subjects affected / exposed	1 / 31 (3.23%)	0 / 170 (0.00%)	0 / 1 (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
Cholecystitis			
subjects affected / exposed	1 / 31 (3.23%)	0 / 170 (0.00%)	0 / 1 (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
Drug-induced liver injury			
subjects affected / exposed	0 / 31 (0.00%)	1 / 170 (0.59%)	0 / 1 (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
Hepatitis			
subjects affected / exposed	0 / 31 (0.00%)	2 / 170 (1.18%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatotoxicity			
subjects affected / exposed	0 / 31 (0.00%)	1 / 170 (0.59%)	0 / 1 (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
Hepatitis acute			
subjects affected / exposed	0 / 31 (0.00%)	1 / 170 (0.59%)	0 / 1 (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
Skin and subcutaneous tissue disorders			
Drug eruption			
subjects affected / exposed	0 / 31 (0.00%)	0 / 170 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			

Acute kidney injury			
subjects affected / exposed	1 / 31 (3.23%)	3 / 170 (1.76%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 2	2 / 3	0 / 0
deaths causally related to treatment / all	0 / 1	1 / 1	0 / 0
Haematuria			
subjects affected / exposed	0 / 31 (0.00%)	1 / 170 (0.59%)	0 / 1 (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 retention			
subjects affected / exposed	1 / 31 (3.23%)	0 / 170 (0.00%)	0 / 1 (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
Renal failure			
subjects affected / exposed	0 / 31 (0.00%)	1 / 170 (0.59%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
Adrenal insufficiency			
subjects affected / exposed	0 / 31 (0.00%)	3 / 170 (1.76%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	3 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypophysitis			
subjects affected / exposed	0 / 31 (0.00%)	4 / 170 (2.35%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	5 / 5	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thyroiditis			
subjects affected / exposed	1 / 31 (3.23%)	0 / 170 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 31 (3.23%)	2 / 170 (1.18%)	0 / 1 (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

Arthralgia			
subjects affected / exposed	0 / 31 (0.00%)	2 / 170 (1.18%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Muscular weakness			
subjects affected / exposed	0 / 31 (0.00%)	1 / 170 (0.59%)	0 / 1 (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
Musculoskeletal pain			
subjects affected / exposed	0 / 31 (0.00%)	1 / 170 (0.59%)	0 / 1 (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
Myositis			
subjects affected / exposed	0 / 31 (0.00%)	2 / 170 (1.18%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain in extremity			
subjects affected / exposed	0 / 31 (0.00%)	1 / 170 (0.59%)	0 / 1 (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
Neck pain			
subjects affected / exposed	0 / 31 (0.00%)	1 / 170 (0.59%)	0 / 1 (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
Infections and infestations			
Cytomegalovirus infection			
subjects affected / exposed	0 / 31 (0.00%)	1 / 170 (0.59%)	0 / 1 (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
Brain abscess			
subjects affected / exposed	0 / 31 (0.00%)	1 / 170 (0.59%)	0 / 1 (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
Diverticulitis			

subjects affected / exposed	0 / 31 (0.00%)	1 / 170 (0.59%)	0 / 1 (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
Empyema			
subjects affected / exposed	0 / 31 (0.00%)	0 / 170 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Encephalitis			
subjects affected / exposed	1 / 31 (3.23%)	0 / 170 (0.00%)	0 / 1 (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
Gastroenteritis			
subjects affected / exposed	0 / 31 (0.00%)	1 / 170 (0.59%)	0 / 1 (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
Pneumonia			
subjects affected / exposed	0 / 31 (0.00%)	10 / 170 (5.88%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	3 / 13	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Klebsiella sepsis			
subjects affected / exposed	0 / 31 (0.00%)	1 / 170 (0.59%)	0 / 1 (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
Oral fungal infection			
subjects affected / exposed	0 / 31 (0.00%)	1 / 170 (0.59%)	0 / 1 (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
Osteomyelitis			
subjects affected / exposed	0 / 31 (0.00%)	1 / 170 (0.59%)	0 / 1 (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
Herpes zoster			

subjects affected / exposed	0 / 31 (0.00%)	1 / 170 (0.59%)	0 / 1 (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
Pneumonia bacterial			
subjects affected / exposed	1 / 31 (3.23%)	0 / 170 (0.00%)	0 / 1 (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 pneumococcal			
subjects affected / exposed	0 / 31 (0.00%)	1 / 170 (0.59%)	0 / 1 (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
Respiratory tract infection			
subjects affected / exposed	0 / 31 (0.00%)	2 / 170 (1.18%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic shock			
subjects affected / exposed	0 / 31 (0.00%)	1 / 170 (0.59%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Urinary tract infection			
subjects affected / exposed	1 / 31 (3.23%)	1 / 170 (0.59%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 0
Sepsis			
subjects affected / exposed	1 / 31 (3.23%)	3 / 170 (1.76%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 0
Metabolism and nutrition disorders			
Acidosis			
subjects affected / exposed	0 / 31 (0.00%)	0 / 170 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dehydration			

subjects affected / exposed	0 / 31 (0.00%)	3 / 170 (1.76%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Diabetes mellitus			
subjects affected / exposed	1 / 31 (3.23%)	0 / 170 (0.00%)	0 / 1 (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
Diabetic ketoacidosis			
subjects affected / exposed	0 / 31 (0.00%)	1 / 170 (0.59%)	0 / 1 (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
Hypoglycaemia			
subjects affected / exposed	0 / 31 (0.00%)	0 / 170 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperglycaemia			
subjects affected / exposed	0 / 31 (0.00%)	0 / 170 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypercalcaemia			
subjects affected / exposed	0 / 31 (0.00%)	2 / 170 (1.18%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypokalaemia			
subjects affected / exposed	0 / 31 (0.00%)	1 / 170 (0.59%)	0 / 1 (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
Hyponatraemia			
subjects affected / exposed	0 / 31 (0.00%)	3 / 170 (1.76%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypomagnesaemia			

subjects affected / exposed	0 / 31 (0.00%)	1 / 170 (0.59%)	0 / 1 (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

Serious adverse events	PART 1: PD-L1-Status		
Total subjects affected by serious adverse events			
subjects affected / exposed	14 / 28 (50.00%)		
number of deaths (all causes)	22		
number of deaths resulting from adverse events	5		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignant neoplasm progression			
subjects affected / exposed	5 / 28 (17.86%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 5		
Cancer pain			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Malignant pleural effusion			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Phaeochromocytoma			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Non-small cell lung cancer			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Neoplasm progression			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Metastases to central nervous system				
subjects affected / exposed	0 / 28 (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 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Tumour ulceration				
subjects affected / exposed	1 / 28 (3.57%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Tumour necrosis				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vascular disorders				
Hypotension				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Embolism				
subjects affected / exposed	1 / 28 (3.57%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
General disorders and administration site conditions				
Fatigue				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Asthenia				

subjects affected / exposed	0 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Chest pain				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Death				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Adverse drug reaction				
subjects affected / exposed	0 / 28 (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 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Inflammation				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Non-cardiac chest pain				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Systemic inflammatory response syndrome				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Performance status decreased				

subjects affected / exposed	0 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pyrexia				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Sudden death				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pain				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Immune system disorders				
Hypersensitivity				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Reproductive system and breast disorders				
Adnexa uteri mass				
subjects affected / exposed	1 / 28 (3.57%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Acute respiratory failure				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Chronic obstructive pulmonary disease				

subjects affected / exposed	0 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Dyspnoea				
subjects affected / exposed	3 / 28 (10.71%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Epistaxis				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pulmonary embolism				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypoxia				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Immune-mediated lung disease				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pleural effusion				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonitis				
subjects affected / exposed	2 / 28 (7.14%)			
occurrences causally related to treatment / all	3 / 3			
deaths causally related to treatment / all	0 / 0			
Pulmonary haemorrhage				

subjects affected / exposed	0 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pulmonary oedema				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory distress				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory failure				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Psychiatric disorders				
Confusional state				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Investigations				
Alanine aminotransferase increased				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Amylase increased				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Aspartate aminotransferase increased				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Blood bilirubin increased				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
General physical condition abnormal				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lipase increased				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Troponin I increased				
subjects affected / exposed	1 / 28 (3.57%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Blood creatinine increased				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Injury, poisoning and procedural complications				
Compression fracture				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Brachial plexus injury				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Depressed fracture				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Fall				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hip fracture				
subjects affected / exposed	1 / 28 (3.57%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Infusion related reaction				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Tendon rupture				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
Atrial fibrillation				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Atrial flutter				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac arrest				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac tamponade				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Tachycardia				

subjects affected / exposed	0 / 28 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nodal rhythm			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pericardial effusion			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Sinus tachycardia			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardio-respiratory arrest			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cerebrovascular accident			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hemiparesis			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Headache			

subjects affected / exposed	0 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Encephalitis autoimmune				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ischaemic stroke				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Radiculopathy				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Metabolic encephalopathy				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Neuralgia				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Polyneuropathy				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lethargy				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Syncope				

subjects affected / exposed	0 / 28 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Thrombocytopenia			
subjects affected / exposed	0 / 28 (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 / 28 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Diarrhoea			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Ascites			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Autoimmune pancreatitis			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Constipation			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Anal fissure			

subjects affected / exposed	0 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Dysphagia				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Enterocolitis				
subjects affected / exposed	1 / 28 (3.57%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Gastric haemorrhage				
subjects affected / exposed	1 / 28 (3.57%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Nausea				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Immune-mediated enterocolitis				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Intestinal obstruction				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Intestinal perforation				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastritis				

subjects affected / exposed	1 / 28 (3.57%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pancreatitis				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Rectal haemorrhage				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vomiting				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hepatobiliary disorders				
Autoimmune hepatitis				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cholecystitis				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Drug-induced liver injury				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hepatitis				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hepatotoxicity				

subjects affected / exposed	0 / 28 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatitis acute			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Drug eruption			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Haematuria			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Urinary retention			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal failure			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Endocrine disorders			
Adrenal insufficiency			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Hypophysitis			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Thyroiditis			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Arthralgia			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Muscular weakness			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal pain			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Myositis			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pain in extremity			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Neck pain			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Cytomegalovirus infection			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Brain abscess			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Diverticulitis			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Empyema			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Encephalitis			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastroenteritis			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Klebsiella sepsis			

subjects affected / exposed	0 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Oral fungal infection				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Osteomyelitis				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Herpes zoster				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia bacterial				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia pneumococcal				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory tract infection				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Septic shock				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Urinary tract infection				

subjects affected / exposed	2 / 28 (7.14%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Sepsis				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Metabolism and nutrition disorders				
Acidosis				
subjects affected / exposed	1 / 28 (3.57%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Dehydration				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Diabetes mellitus				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Diabetic ketoacidosis				
subjects affected / exposed	1 / 28 (3.57%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hypoglycaemia				
subjects affected / exposed	1 / 28 (3.57%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Hyperglycaemia				
subjects affected / exposed	1 / 28 (3.57%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hypercalcaemia				

subjects affected / exposed	1 / 28 (3.57%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hypokalaemia				
subjects affected / exposed	2 / 28 (7.14%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Hyponatraemia				
subjects affected / exposed	1 / 28 (3.57%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Hypomagnesaemia				
subjects affected / exposed	0 / 28 (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	PART 1: PD-L1+ Status	PART 2: PD-L1 Status Independent	PART 1: Not Evaluable/Indeterminate PD-L1 Status
Total subjects affected by non-serious adverse events			
subjects affected / exposed	31 / 31 (100.00%)	161 / 170 (94.71%)	1 / 1 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour pain			
subjects affected / exposed	3 / 31 (9.68%)	1 / 170 (0.59%)	0 / 1 (0.00%)
occurrences (all)	3	1	0
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 31 (0.00%)	7 / 170 (4.12%)	0 / 1 (0.00%)
occurrences (all)	0	11	0
Hot flush			
subjects affected / exposed	1 / 31 (3.23%)	2 / 170 (1.18%)	0 / 1 (0.00%)
occurrences (all)	1	2	0
Hypotension			

subjects affected / exposed	3 / 31 (9.68%)	7 / 170 (4.12%)	0 / 1 (0.00%)
occurrences (all)	4	8	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 31 (3.23%)	20 / 170 (11.76%)	0 / 1 (0.00%)
occurrences (all)	1	30	0
Chills			
subjects affected / exposed	2 / 31 (6.45%)	9 / 170 (5.29%)	0 / 1 (0.00%)
occurrences (all)	2	9	0
Fatigue			
subjects affected / exposed	18 / 31 (58.06%)	43 / 170 (25.29%)	0 / 1 (0.00%)
occurrences (all)	19	51	0
Gait disturbance			
subjects affected / exposed	0 / 31 (0.00%)	1 / 170 (0.59%)	0 / 1 (0.00%)
occurrences (all)	0	1	0
Malaise			
subjects affected / exposed	2 / 31 (6.45%)	4 / 170 (2.35%)	0 / 1 (0.00%)
occurrences (all)	2	5	0
Oedema peripheral			
subjects affected / exposed	4 / 31 (12.90%)	18 / 170 (10.59%)	0 / 1 (0.00%)
occurrences (all)	4	22	0
Pyrexia			
subjects affected / exposed	5 / 31 (16.13%)	27 / 170 (15.88%)	0 / 1 (0.00%)
occurrences (all)	6	38	0
Non-cardiac chest pain			
subjects affected / exposed	1 / 31 (3.23%)	12 / 170 (7.06%)	0 / 1 (0.00%)
occurrences (all)	1	13	0
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 31 (0.00%)	2 / 170 (1.18%)	0 / 1 (0.00%)
occurrences (all)	0	5	0
Reproductive system and breast disorders			
Pelvic pain			
subjects affected / exposed	2 / 31 (6.45%)	0 / 170 (0.00%)	0 / 1 (0.00%)
occurrences (all)	2	0	0
Respiratory, thoracic and mediastinal			

disorders			
Cough			
subjects affected / exposed	4 / 31 (12.90%)	45 / 170 (26.47%)	0 / 1 (0.00%)
occurrences (all)	6	58	0
Dyspnoea			
subjects affected / exposed	8 / 31 (25.81%)	45 / 170 (26.47%)	0 / 1 (0.00%)
occurrences (all)	9	56	0
Wheezing			
subjects affected / exposed	0 / 31 (0.00%)	2 / 170 (1.18%)	0 / 1 (0.00%)
occurrences (all)	0	2	0
Sinus congestion			
subjects affected / exposed	1 / 31 (3.23%)	1 / 170 (0.59%)	0 / 1 (0.00%)
occurrences (all)	1	1	0
Productive cough			
subjects affected / exposed	3 / 31 (9.68%)	17 / 170 (10.00%)	0 / 1 (0.00%)
occurrences (all)	4	21	0
Pneumonitis			
subjects affected / exposed	5 / 31 (16.13%)	10 / 170 (5.88%)	0 / 1 (0.00%)
occurrences (all)	5	10	0
Oropharyngeal pain			
subjects affected / exposed	1 / 31 (3.23%)	3 / 170 (1.76%)	0 / 1 (0.00%)
occurrences (all)	1	3	0
Nasal congestion			
subjects affected / exposed	0 / 31 (0.00%)	3 / 170 (1.76%)	0 / 1 (0.00%)
occurrences (all)	0	3	0
Dyspnoea exertional			
subjects affected / exposed	4 / 31 (12.90%)	3 / 170 (1.76%)	0 / 1 (0.00%)
occurrences (all)	4	4	0
Epistaxis			
subjects affected / exposed	0 / 31 (0.00%)	5 / 170 (2.94%)	0 / 1 (0.00%)
occurrences (all)	0	5	0
Haemoptysis			
subjects affected / exposed	4 / 31 (12.90%)	8 / 170 (4.71%)	0 / 1 (0.00%)
occurrences (all)	4	12	0
Hypoxia			

subjects affected / exposed	7 / 31 (22.58%)	1 / 170 (0.59%)	0 / 1 (0.00%)
occurrences (all)	7	1	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	4 / 31 (12.90%)	5 / 170 (2.94%)	0 / 1 (0.00%)
occurrences (all)	4	6	0
Confusional state			
subjects affected / exposed	2 / 31 (6.45%)	5 / 170 (2.94%)	0 / 1 (0.00%)
occurrences (all)	3	5	0
Depression			
subjects affected / exposed	1 / 31 (3.23%)	8 / 170 (4.71%)	0 / 1 (0.00%)
occurrences (all)	1	8	0
Insomnia			
subjects affected / exposed	2 / 31 (6.45%)	12 / 170 (7.06%)	0 / 1 (0.00%)
occurrences (all)	2	12	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	7 / 31 (22.58%)	30 / 170 (17.65%)	0 / 1 (0.00%)
occurrences (all)	8	43	0
Amylase increased			
subjects affected / exposed	6 / 31 (19.35%)	29 / 170 (17.06%)	0 / 1 (0.00%)
occurrences (all)	8	64	0
Aspartate aminotransferase increased			
subjects affected / exposed	7 / 31 (22.58%)	33 / 170 (19.41%)	0 / 1 (0.00%)
occurrences (all)	9	48	0
Platelet count decreased			
subjects affected / exposed	2 / 31 (6.45%)	4 / 170 (2.35%)	0 / 1 (0.00%)
occurrences (all)	2	4	0
Blood bicarbonate decreased			
subjects affected / exposed	0 / 31 (0.00%)	0 / 170 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Blood bilirubin increased			
subjects affected / exposed	1 / 31 (3.23%)	1 / 170 (0.59%)	0 / 1 (0.00%)
occurrences (all)	2	1	0
Blood creatinine increased			

subjects affected / exposed	3 / 31 (9.68%)	22 / 170 (12.94%)	0 / 1 (0.00%)
occurrences (all)	5	35	0
International normalised ratio increased			
subjects affected / exposed	2 / 31 (6.45%)	0 / 170 (0.00%)	0 / 1 (0.00%)
occurrences (all)	2	0	0
Lipase increased			
subjects affected / exposed	6 / 31 (19.35%)	28 / 170 (16.47%)	0 / 1 (0.00%)
occurrences (all)	7	45	0
Blood alkaline phosphatase increased			
subjects affected / exposed	3 / 31 (9.68%)	22 / 170 (12.94%)	0 / 1 (0.00%)
occurrences (all)	3	34	0
Weight decreased			
subjects affected / exposed	3 / 31 (9.68%)	20 / 170 (11.76%)	0 / 1 (0.00%)
occurrences (all)	3	22	0
White blood cell count decreased			
subjects affected / exposed	2 / 31 (6.45%)	3 / 170 (1.76%)	0 / 1 (0.00%)
occurrences (all)	4	6	0
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	2 / 31 (6.45%)	5 / 170 (2.94%)	0 / 1 (0.00%)
occurrences (all)	2	5	0
Cardiac disorders			
Sinus tachycardia			
subjects affected / exposed	2 / 31 (6.45%)	2 / 170 (1.18%)	0 / 1 (0.00%)
occurrences (all)	3	2	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	5 / 31 (16.13%)	12 / 170 (7.06%)	0 / 1 (0.00%)
occurrences (all)	6	15	0
Amnesia			
subjects affected / exposed	3 / 31 (9.68%)	1 / 170 (0.59%)	0 / 1 (0.00%)
occurrences (all)	3	1	0
Neuropathy peripheral			
subjects affected / exposed	2 / 31 (6.45%)	1 / 170 (0.59%)	0 / 1 (0.00%)
occurrences (all)	2	1	0
Dysgeusia			

subjects affected / exposed	0 / 31 (0.00%)	8 / 170 (4.71%)	0 / 1 (0.00%)
occurrences (all)	0	9	0
Headache			
subjects affected / exposed	4 / 31 (12.90%)	25 / 170 (14.71%)	0 / 1 (0.00%)
occurrences (all)	7	32	0
Peroneal nerve palsy			
subjects affected / exposed	0 / 31 (0.00%)	0 / 170 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	5 / 31 (16.13%)	37 / 170 (21.76%)	0 / 1 (0.00%)
occurrences (all)	7	56	0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	2 / 31 (6.45%)	8 / 170 (4.71%)	0 / 1 (0.00%)
occurrences (all)	2	12	0
Abdominal pain upper			
subjects affected / exposed	1 / 31 (3.23%)	7 / 170 (4.12%)	0 / 1 (0.00%)
occurrences (all)	1	8	0
Colitis			
subjects affected / exposed	0 / 31 (0.00%)	4 / 170 (2.35%)	0 / 1 (0.00%)
occurrences (all)	0	4	0
Constipation			
subjects affected / exposed	6 / 31 (19.35%)	25 / 170 (14.71%)	0 / 1 (0.00%)
occurrences (all)	6	31	0
Stomatitis			
subjects affected / exposed	1 / 31 (3.23%)	8 / 170 (4.71%)	0 / 1 (0.00%)
occurrences (all)	1	8	0
Dry mouth			
subjects affected / exposed	1 / 31 (3.23%)	12 / 170 (7.06%)	0 / 1 (0.00%)
occurrences (all)	1	12	0
Dyspepsia			
subjects affected / exposed	0 / 31 (0.00%)	7 / 170 (4.12%)	0 / 1 (0.00%)
occurrences (all)	0	7	0
Dysphagia			

subjects affected / exposed	0 / 31 (0.00%)	14 / 170 (8.24%)	0 / 1 (0.00%)
occurrences (all)	0	16	0
Flatulence			
subjects affected / exposed	0 / 31 (0.00%)	3 / 170 (1.76%)	0 / 1 (0.00%)
occurrences (all)	0	3	0
Gastrooesophageal reflux disease			
subjects affected / exposed	3 / 31 (9.68%)	4 / 170 (2.35%)	0 / 1 (0.00%)
occurrences (all)	3	5	0
Nausea			
subjects affected / exposed	12 / 31 (38.71%)	48 / 170 (28.24%)	0 / 1 (0.00%)
occurrences (all)	14	57	0
Diarrhoea			
subjects affected / exposed	7 / 31 (22.58%)	65 / 170 (38.24%)	0 / 1 (0.00%)
occurrences (all)	9	108	0
Vomiting			
subjects affected / exposed	4 / 31 (12.90%)	20 / 170 (11.76%)	0 / 1 (0.00%)
occurrences (all)	5	23	0
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	3 / 31 (9.68%)	2 / 170 (1.18%)	0 / 1 (0.00%)
occurrences (all)	3	2	0
Pruritus			
subjects affected / exposed	6 / 31 (19.35%)	43 / 170 (25.29%)	1 / 1 (100.00%)
occurrences (all)	10	78	1
Night sweats			
subjects affected / exposed	2 / 31 (6.45%)	5 / 170 (2.94%)	0 / 1 (0.00%)
occurrences (all)	2	6	0
Dry skin			
subjects affected / exposed	1 / 31 (3.23%)	15 / 170 (8.82%)	0 / 1 (0.00%)
occurrences (all)	1	15	0
Rash maculo-papular			
subjects affected / exposed	3 / 31 (9.68%)	4 / 170 (2.35%)	0 / 1 (0.00%)
occurrences (all)	3	4	0
Rash			
subjects affected / exposed	7 / 31 (22.58%)	42 / 170 (24.71%)	0 / 1 (0.00%)
occurrences (all)	10	74	0

Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 31 (3.23%)	3 / 170 (1.76%)	0 / 1 (0.00%)
occurrences (all)	1	3	0
Haematuria			
subjects affected / exposed	0 / 31 (0.00%)	3 / 170 (1.76%)	0 / 1 (0.00%)
occurrences (all)	0	3	0
Pollakiuria			
subjects affected / exposed	0 / 31 (0.00%)	2 / 170 (1.18%)	0 / 1 (0.00%)
occurrences (all)	0	3	0
Endocrine disorders			
Hyperthyroidism			
subjects affected / exposed	1 / 31 (3.23%)	16 / 170 (9.41%)	0 / 1 (0.00%)
occurrences (all)	1	16	0
Hypothyroidism			
subjects affected / exposed	4 / 31 (12.90%)	15 / 170 (8.82%)	0 / 1 (0.00%)
occurrences (all)	4	15	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	5 / 31 (16.13%)	25 / 170 (14.71%)	0 / 1 (0.00%)
occurrences (all)	6	34	0
Back pain			
subjects affected / exposed	5 / 31 (16.13%)	18 / 170 (10.59%)	0 / 1 (0.00%)
occurrences (all)	5	24	0
Flank pain			
subjects affected / exposed	0 / 31 (0.00%)	2 / 170 (1.18%)	0 / 1 (0.00%)
occurrences (all)	0	2	0
Muscular weakness			
subjects affected / exposed	2 / 31 (6.45%)	2 / 170 (1.18%)	0 / 1 (0.00%)
occurrences (all)	3	2	0
Neck pain			
subjects affected / exposed	2 / 31 (6.45%)	7 / 170 (4.12%)	0 / 1 (0.00%)
occurrences (all)	2	7	0
Pain in extremity			
subjects affected / exposed	1 / 31 (3.23%)	9 / 170 (5.29%)	0 / 1 (0.00%)
occurrences (all)	1	9	0

Myalgia			
subjects affected / exposed	2 / 31 (6.45%)	14 / 170 (8.24%)	0 / 1 (0.00%)
occurrences (all)	2	16	0
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	0 / 31 (0.00%)	5 / 170 (2.94%)	0 / 1 (0.00%)
occurrences (all)	0	5	0
Conjunctivitis			
subjects affected / exposed	2 / 31 (6.45%)	2 / 170 (1.18%)	0 / 1 (0.00%)
occurrences (all)	2	3	0
Nasopharyngitis			
subjects affected / exposed	2 / 31 (6.45%)	9 / 170 (5.29%)	0 / 1 (0.00%)
occurrences (all)	2	11	0
Sinusitis			
subjects affected / exposed	2 / 31 (6.45%)	3 / 170 (1.76%)	0 / 1 (0.00%)
occurrences (all)	3	3	0
Urinary tract infection			
subjects affected / exposed	5 / 31 (16.13%)	4 / 170 (2.35%)	0 / 1 (0.00%)
occurrences (all)	5	4	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	9 / 31 (29.03%)	38 / 170 (22.35%)	0 / 1 (0.00%)
occurrences (all)	9	48	0
Dehydration			
subjects affected / exposed	2 / 31 (6.45%)	2 / 170 (1.18%)	0 / 1 (0.00%)
occurrences (all)	2	2	0
Hypercalcaemia			
subjects affected / exposed	0 / 31 (0.00%)	6 / 170 (3.53%)	0 / 1 (0.00%)
occurrences (all)	0	6	0
Hyperglycaemia			
subjects affected / exposed	2 / 31 (6.45%)	19 / 170 (11.18%)	0 / 1 (0.00%)
occurrences (all)	3	28	0
Hyponatraemia			
subjects affected / exposed	4 / 31 (12.90%)	16 / 170 (9.41%)	0 / 1 (0.00%)
occurrences (all)	6	21	0
Hypoalbuminaemia			

subjects affected / exposed	2 / 31 (6.45%)	12 / 170 (7.06%)	0 / 1 (0.00%)
occurrences (all)	4	19	0
Hypocalcaemia			
subjects affected / exposed	3 / 31 (9.68%)	2 / 170 (1.18%)	0 / 1 (0.00%)
occurrences (all)	6	3	0
Hypoglycaemia			
subjects affected / exposed	0 / 31 (0.00%)	0 / 170 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Hypokalaemia			
subjects affected / exposed	5 / 31 (16.13%)	12 / 170 (7.06%)	0 / 1 (0.00%)
occurrences (all)	13	13	0
Hypomagnesaemia			
subjects affected / exposed	2 / 31 (6.45%)	8 / 170 (4.71%)	0 / 1 (0.00%)
occurrences (all)	3	16	0
Hyperkalaemia			
subjects affected / exposed	1 / 31 (3.23%)	5 / 170 (2.94%)	0 / 1 (0.00%)
occurrences (all)	1	5	0
Hypophosphataemia			
subjects affected / exposed	1 / 31 (3.23%)	1 / 170 (0.59%)	0 / 1 (0.00%)
occurrences (all)	1	1	0

Non-serious adverse events	PART 1: PD-L1-Status		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	27 / 28 (96.43%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour pain			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Vascular disorders			
Hypertension			
subjects affected / exposed	5 / 28 (17.86%)		
occurrences (all)	10		
Hot flush			
subjects affected / exposed	2 / 28 (7.14%)		
occurrences (all)	4		
Hypotension			

subjects affected / exposed	4 / 28 (14.29%)		
occurrences (all)	4		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	2 / 28 (7.14%)		
occurrences (all)	2		
Chills			
subjects affected / exposed	2 / 28 (7.14%)		
occurrences (all)	2		
Fatigue			
subjects affected / exposed	16 / 28 (57.14%)		
occurrences (all)	19		
Gait disturbance			
subjects affected / exposed	2 / 28 (7.14%)		
occurrences (all)	2		
Malaise			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Oedema peripheral			
subjects affected / exposed	3 / 28 (10.71%)		
occurrences (all)	3		
Pyrexia			
subjects affected / exposed	5 / 28 (17.86%)		
occurrences (all)	6		
Non-cardiac chest pain			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	2 / 28 (7.14%)		
occurrences (all)	3		
Reproductive system and breast disorders			
Pelvic pain			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal			

disorders				
Cough				
subjects affected / exposed	10 / 28 (35.71%)			
occurrences (all)	13			
Dyspnoea				
subjects affected / exposed	12 / 28 (42.86%)			
occurrences (all)	12			
Wheezing				
subjects affected / exposed	2 / 28 (7.14%)			
occurrences (all)	2			
Sinus congestion				
subjects affected / exposed	2 / 28 (7.14%)			
occurrences (all)	2			
Productive cough				
subjects affected / exposed	3 / 28 (10.71%)			
occurrences (all)	4			
Pneumonitis				
subjects affected / exposed	2 / 28 (7.14%)			
occurrences (all)	2			
Oropharyngeal pain				
subjects affected / exposed	2 / 28 (7.14%)			
occurrences (all)	2			
Nasal congestion				
subjects affected / exposed	3 / 28 (10.71%)			
occurrences (all)	4			
Dyspnoea exertional				
subjects affected / exposed	3 / 28 (10.71%)			
occurrences (all)	3			
Epistaxis				
subjects affected / exposed	3 / 28 (10.71%)			
occurrences (all)	4			
Haemoptysis				
subjects affected / exposed	0 / 28 (0.00%)			
occurrences (all)	0			
Hypoxia				

subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	2		
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Confusional state			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Depression			
subjects affected / exposed	2 / 28 (7.14%)		
occurrences (all)	2		
Insomnia			
subjects affected / exposed	5 / 28 (17.86%)		
occurrences (all)	7		
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	2 / 28 (7.14%)		
occurrences (all)	2		
Amylase increased			
subjects affected / exposed	5 / 28 (17.86%)		
occurrences (all)	6		
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	3		
Platelet count decreased			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Blood bicarbonate decreased			
subjects affected / exposed	2 / 28 (7.14%)		
occurrences (all)	3		
Blood bilirubin increased			
subjects affected / exposed	2 / 28 (7.14%)		
occurrences (all)	2		
Blood creatinine increased			

subjects affected / exposed	3 / 28 (10.71%)		
occurrences (all)	7		
International normalised ratio increased			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Lipase increased			
subjects affected / exposed	7 / 28 (25.00%)		
occurrences (all)	10		
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	2		
Weight decreased			
subjects affected / exposed	2 / 28 (7.14%)		
occurrences (all)	2		
White blood cell count decreased			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	2 / 28 (7.14%)		
occurrences (all)	4		
Cardiac disorders			
Sinus tachycardia			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Dizziness			
subjects affected / exposed	3 / 28 (10.71%)		
occurrences (all)	5		
Amnesia			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Neuropathy peripheral			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Dysgeusia			

subjects affected / exposed	2 / 28 (7.14%)		
occurrences (all)	2		
Headache			
subjects affected / exposed	5 / 28 (17.86%)		
occurrences (all)	7		
Peroneal nerve palsy			
subjects affected / exposed	2 / 28 (7.14%)		
occurrences (all)	2		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	6 / 28 (21.43%)		
occurrences (all)	6		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	3 / 28 (10.71%)		
occurrences (all)	3		
Abdominal pain upper			
subjects affected / exposed	2 / 28 (7.14%)		
occurrences (all)	2		
Colitis			
subjects affected / exposed	2 / 28 (7.14%)		
occurrences (all)	2		
Constipation			
subjects affected / exposed	9 / 28 (32.14%)		
occurrences (all)	9		
Stomatitis			
subjects affected / exposed	2 / 28 (7.14%)		
occurrences (all)	3		
Dry mouth			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Dyspepsia			
subjects affected / exposed	4 / 28 (14.29%)		
occurrences (all)	4		
Dysphagia			

subjects affected / exposed	3 / 28 (10.71%)		
occurrences (all)	3		
Flatulence			
subjects affected / exposed	2 / 28 (7.14%)		
occurrences (all)	2		
Gastrooesophageal reflux disease			
subjects affected / exposed	2 / 28 (7.14%)		
occurrences (all)	2		
Nausea			
subjects affected / exposed	11 / 28 (39.29%)		
occurrences (all)	14		
Diarrhoea			
subjects affected / exposed	12 / 28 (42.86%)		
occurrences (all)	20		
Vomiting			
subjects affected / exposed	6 / 28 (21.43%)		
occurrences (all)	6		
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Pruritus			
subjects affected / exposed	10 / 28 (35.71%)		
occurrences (all)	13		
Night sweats			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Dry skin			
subjects affected / exposed	3 / 28 (10.71%)		
occurrences (all)	4		
Rash maculo-papular			
subjects affected / exposed	6 / 28 (21.43%)		
occurrences (all)	8		
Rash			
subjects affected / exposed	8 / 28 (28.57%)		
occurrences (all)	9		

Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	2 / 28 (7.14%)		
occurrences (all)	2		
Haematuria			
subjects affected / exposed	3 / 28 (10.71%)		
occurrences (all)	4		
Pollakiuria			
subjects affected / exposed	4 / 28 (14.29%)		
occurrences (all)	4		
Endocrine disorders			
Hyperthyroidism			
subjects affected / exposed	2 / 28 (7.14%)		
occurrences (all)	2		
Hypothyroidism			
subjects affected / exposed	5 / 28 (17.86%)		
occurrences (all)	5		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	3 / 28 (10.71%)		
occurrences (all)	5		
Back pain			
subjects affected / exposed	2 / 28 (7.14%)		
occurrences (all)	3		
Flank pain			
subjects affected / exposed	3 / 28 (10.71%)		
occurrences (all)	3		
Muscular weakness			
subjects affected / exposed	7 / 28 (25.00%)		
occurrences (all)	8		
Neck pain			
subjects affected / exposed	2 / 28 (7.14%)		
occurrences (all)	2		
Pain in extremity			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		

Myalgia subjects affected / exposed occurrences (all)	2 / 28 (7.14%) 2		
Infections and infestations Upper respiratory tract infection subjects affected / exposed occurrences (all)	3 / 28 (10.71%) 3		
Conjunctivitis subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0		
Nasopharyngitis subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0		
Sinusitis subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0		
Urinary tract infection subjects affected / exposed occurrences (all)	5 / 28 (17.86%) 5		
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	9 / 28 (32.14%) 10		
Dehydration subjects affected / exposed occurrences (all)	3 / 28 (10.71%) 4		
Hypercalcaemia subjects affected / exposed occurrences (all)	2 / 28 (7.14%) 2		
Hyperglycaemia subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0		
Hyponatraemia subjects affected / exposed occurrences (all)	4 / 28 (14.29%) 5		
Hypoalbuminaemia			

subjects affected / exposed	3 / 28 (10.71%)		
occurrences (all)	4		
Hypocalcaemia			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	2		
Hypoglycaemia			
subjects affected / exposed	3 / 28 (10.71%)		
occurrences (all)	3		
Hypokalaemia			
subjects affected / exposed	4 / 28 (14.29%)		
occurrences (all)	7		
Hypomagnesaemia			
subjects affected / exposed	3 / 28 (10.71%)		
occurrences (all)	5		
Hyperkalaemia			
subjects affected / exposed	2 / 28 (7.14%)		
occurrences (all)	2		
Hypophosphataemia			
subjects affected / exposed	2 / 28 (7.14%)		
occurrences (all)	3		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
03 November 2016	Schedule of Activities Update
29 March 2017	Endpoints Update
02 March 2018	Inclusion Criteria Update
03 May 2019	Endpoints update
18 December 2019	Inclusion/Exclusion Criteria Update

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported