Clinical trial results:
A Randomized Phase 2 Study of the Combination of Pembrolizumab (MK- 3475) Plus Epacadostat (INCB024360) with Platinum-based Chemotherapy Versus Pembrolizumab Plus Platinum-based Chemotherapy Plus Placebo as First-Line Treatment in Patients with Metastatic Non-Small Cell Lung Cancer

Summary

EudraCT number	2017-001810-27
Trial protocol	IE ES DE HU GB FR IT
Global end of trial date	16 October 2020

Results information

Result version number	v1 (current)
This version publication date	04 December 2021
First version publication date	04 December 2021

Trial information

Trial identification

Sponsor protocol code	KEYNOTE-715-06/ECHO-306-06

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Incyte
Sponsor organisation address	1801 Augustine Cutoff drive, Wilmington, United States, 19803
Public contact	Study Director, Incyte Corporation, +1 8554633463, medinfo@incyte.com
Scientific contact	Study Director, Incyte Corporation, +1 8554633463, medinfo@incyte.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	16 October 2020
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	16 October 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The purpose of this study was to evaluate the efficacy and safety of pembrolizumab plus epacadostat with platinum-based chemotherapy versus pembrolizumab plus platinum-based chemotherapy plus placebo as first-line therapy in participants with metastatic non-small cell lung cancer (NSCLC).

Protection of trial subjects:

This study was conducted in conformance with applicable country or local requirements regarding ethical committee review, informed consent, and other statutes or regulations regarding the protection of the rights and welfare of human participants in biomedical research.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	09 January 2018
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 39
Country: Number of subjects enrolled	Canada: 13
Country: Number of subjects enrolled	Spain: 15
Country: Number of subjects enrolled	United Kingdom: 7
Country: Number of subjects enrolled	Hungary: 11
Country: Number of subjects enrolled	Israel: 41
Country: Number of subjects enrolled	Italy: 13
Country: Number of subjects enrolled	Mexico: 1
Country: Number of subjects enrolled	Russian Federation: 24
Country: Number of subjects enrolled	Turkey: 27
Country: Number of subjects enrolled	Taiwan: 17
Country: Number of subjects enrolled	United States: 25
Worldwide total number of subjects	233
EEA total number of subjects	39

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	129
From 65 to 84 years	104
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants took part in the study at 65 investigative sites in 12 countries.

Pre-assignment

Screening details:

The original planned enrollment was 1062 participants across 3 treatment arms. With Protocol Amendment 05 the Epacadostat + Pembrolizumab (E+P) arm was dropped, and the planned sample size was reduced to a total of 148 participants randomized into the 2 remaining arms. 233 participants were randomized and 228 participants received study treatment.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Carer, Data analyst

Arms

Are arms mutually exclusive?	Yes
Arm title	Pembrolizumab + Chemotherapy + Epacadostat

Arm description:

Participant received pembrolizumab 200 mg intravenous (IV) infusion, every 3 weeks (Q3W) on Day 1 of each 21 day cycle for up to 35 cycles + epacadostat 100 mg tablets, orally, twice daily (BID) in each 21 day cycle for up to 35 cycles + platinum-doublet chemotherapy (pemetrexed 500 mg/m^2 IV infusion, Q3W + cisplatin 75 mg/m^2 IV infusion, Q3W or carboplatin 5-6 mg/mL/min IV infusion Q3W for 4 cycles followed by pemetrexed maintenance; or paclitaxel 200 mg /m^2 IV infusion, Q3W + carboplatin 5-6 mg/mL/min IV infusion Q3W for 4 cycles).

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

Dosage and administration details:

200 mg every 3 weeks

Investigational medicinal product name	platinum based chemotherapy
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

every 3 weeks

Investigational medicinal product name	epacadostat
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

100 mg twice a day

Arm title	Pembrolizumab + Chemotherapy + Placebo

Arm description:

Participant received pembrolizumab 200 mg IV infusion, Q3W on Day 1 of each 21 day cycle for up to 35 cycles + epacadostat matching placebo tablets, orally, BID in each 21 day cycle for up to 35 cycles + platinum-doublet chemotherapy (pemetrexed 500 mg/m^2 IV infusion, Q3W + cisplatin 75 mg/m^2 IV infusion, Q3W or carboplatin 5-6 mg/mL/min IV infusion Q3W for 4 cycles followed by pemetrexed maintenance; or paclitaxel 200 mg /m^2 IV infusion, Q3W + carboplatin 5-6 mg/mL/min IV infusion Q3W for 4 cycles).

Arm type	Placebo
Investigational medicinal product name	pembrolizumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for injection, Injection
Routes of administration	Intravenous use

Dosage and administration details:

200 mg IV every 3 weeks

Investigational medicinal product name	placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Buccal tablet, Tablet
Routes of administration	Oral use

Dosage and administration details:

twice a day

Investigational medicinal product name	platinum based chemotherapy
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

every 3 weeks

Arm title	Pembrolizumab + Epacadostat

Arm description:

Participant received pembrolizumab 200 mg IV infusion, Q3W on Day 1 of each 21 day cycle for up to 35 cycles + epacadostat 100 mg tablets, orally, BID in each 21 day cycle for up to 35 cycles.

Arm type	Experimental
Investigational medicinal product name	epacadostat
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

100 mg twice a day

Investigational medicinal product name	pembrolizumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

200 mg every 3 weeks

Number of subjects in period 1	Pembrolizumab + Chemotherapy + Epacadostat	Pembrolizumab + Chemotherapy + Placebo	Pembrolizumab + Epacadostat
Started	91	87	55
Completed	46	42	22
Not completed	45	45	33
Adverse event, serious fatal	34	35	23
Physician decision	6	7	2
Consent withdrawn by subject	4	3	6
Study terminated by sponsor	1	-	1
Lost to follow-up	-	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Pembrolizumab + Chemotherapy + Epacadostat
Reporting group description:	
Participant received pembrolizumab 200 mg intravenous (IV) infusion, every 3 weeks (Q3W) on Day 1 of each 21 day cycle for up to 35 cycles + epacadostat 100 mg tablets, orally, twice daily (BID) in each 21 day cycle for up to 35 cycles + platinum-doublet chemotherapy (pemetrexed 500 mg/m^2 IV infusion, Q3W + cisplatin 75 mg/m^2 IV infusion, Q3W or carboplatin 5-6 mg/mL/min IV infusion Q3W for 4 cycles followed by pemetrexed maintenance; or paclitaxel 200 mg /m^2 IV infusion, Q3W + carboplatin 5-6 mg/mL/min IV infusion Q3W for 4 cycles).	
Reporting group title	Pembrolizumab + Chemotherapy + Placebo
Reporting group description:	
Participant received pembrolizumab 200 mg IV infusion, Q3W on Day 1 of each 21 day cycle for up to 35 cycles + epacadostat matching placebo tablets, orally, BID in each 21 day cycle for up to 35 cycles + platinum-doublet chemotherapy (pemetrexed 500 mg/m^2 IV infusion, Q3W + cisplatin 75 mg/m^2 IV infusion, Q3W or carboplatin 5-6 mg/mL/min IV infusion Q3W for 4 cycles followed by pemetrexed maintenance; or paclitaxel 200 mg /m^2 IV infusion, Q3W + carboplatin 5-6 mg/mL/min IV infusion Q3W for 4 cycles).	
Reporting group title	Pembrolizumab + Epacadostat
Reporting group description:	
Participant received pembrolizumab 200 mg IV infusion, Q3W on Day 1 of each 21 day cycle for up to 35 cycles + epacadostat 100 mg tablets, orally, BID in each 21 day cycle for up to 35 cycles.	

Reporting group values	Pembrolizumab + Chemotherapy + Epacadostat	Pembrolizumab + Chemotherapy + Placebo	Pembrolizumab + Epacadostat
Number of subjects	91	87	55
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	49	46	34
From 65-84 years	42	41	21
85 years and over	0	0	0
Age Continuous Units: years			
arithmetic mean	63.0	63.6	62.8
standard deviation	± 11.7	± 8.8	± 8.4
Sex: Female, Male Units:			
Female	33	30	16
Male	58	57	39
Race/Ethnicity, Customized Units: Subjects			
American Indian Or Alaska Native	1	0	0
Asian	11	10	2
Black Or African American	1	1	0

White	78	75	53
Missing	0	1	0
Race/Ethnicity, Customized Units: Subjects			
Hispanic or Latino	3	1	1
Not Hispanic or Latino	86	85	52
Unknown	2	1	1
Not Reported	0	0	1

Reporting group values	Total		
Number of subjects	233		
Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days-23 months)	0		
Children (2-11 years)	0		
Adolescents (12-17 years)	0		
Adults (18-64 years)	129		
From 65-84 years	104		
85 years and over	0		
Age Continuous Units: years			
arithmetic mean			
standard deviation	-		
Sex: Female, Male Units:			
Female	79		
Male	154		
Race/Ethnicity, Customized Units: Subjects			
American Indian Or Alaska Native	1		
Asian	23		
Black Or African American	2		
White	206		
Missing	1		
Race/Ethnicity, Customized Units: Subjects			
Hispanic or Latino	5		
Not Hispanic or Latino	223		
Unknown	4		
Not Reported	1		

End points

End points reporting groups

Reporting group title	Pembrolizumab + Chemotherapy + Epacadostat

Reporting group description:

Participant received pembrolizumab 200 mg intravenous (IV) infusion, every 3 weeks (Q3W) on Day 1 of each 21 day cycle for up to 35 cycles + epacadostat 100 mg tablets, orally, twice daily (BID) in each 21 day cycle for up to 35 cycles + platinum-doublet chemotherapy (pemetrexed 500 mg/m^2 IV infusion, Q3W + cisplatin 75 mg/m^2 IV infusion, Q3W or carboplatin 5-6 mg/mL/min IV infusion Q3W for 4 cycles followed by pemetrexed maintenance; or paclitaxel 200 mg /m^2 IV infusion, Q3W + carboplatin 5-6 mg/mL/min IV infusion Q3W for 4 cycles).

Reporting group title	Pembrolizumab + Chemotherapy + Placebo

Reporting group description:

Participant received pembrolizumab 200 mg IV infusion, Q3W on Day 1 of each 21 day cycle for up to 35 cycles + epacadostat matching placebo tablets, orally, BID in each 21 day cycle for up to 35 cycles + platinum-doublet chemotherapy (pemetrexed 500 mg/m^2 IV infusion, Q3W + cisplatin 75 mg/m^2 IV infusion, Q3W or carboplatin 5-6 mg/mL/min IV infusion Q3W for 4 cycles followed by pemetrexed maintenance; or paclitaxel 200 mg /m^2 IV infusion, Q3W + carboplatin 5-6 mg/mL/min IV infusion Q3W for 4 cycles).

Reporting group title	Pembrolizumab + Epacadostat

Reporting group description:

Participant received pembrolizumab 200 mg IV infusion, Q3W on Day 1 of each 21 day cycle for up to 35 cycles + epacadostat 100 mg tablets, orally, BID in each 21 day cycle for up to 35 cycles.

Primary: Objective Response Rate (ORR) of Pembrolizumab + Chemotherapy + Epacadostat Versus Pembrolizumab + Chemotherapy + Placebo

End point title	Objective Response Rate (ORR) of Pembrolizumab + Chemotherapy + Epacadostat Versus Pembrolizumab + Chemotherapy + Placebo[1]

End point description:

ORR is defined as the percentage of participants who have a confirmed complete response (CR) or partial response (PR) per Response Evaluation Criteria in Solid Tumors (RECIST 1.1) based on blinded independent central review (BICR).

End point type	Primary

End point timeframe:

Assessed every 12 up to 24 months

Notes:

[1] - 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: No statistical analysis for this endpoint.

End point values	Pembrolizumab + Chemotherapy + Epacadostat	Pembrolizumab + Chemotherapy + Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	91	87		
Units: percentage of participants				
number (confidence interval 95%)	26.4 (17.7 to 36.7)	44.8 (34.1 to 55.9)		

Statistical analyses

Statistical analysis title	Stratified Miettinen and Nurminen method
Comparison groups	Pembrolizumab + Chemotherapy + Epacadostat v Pembrolizumab + Chemotherapy + Placebo
Number of subjects included in analysis	178
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.9948 [2]
Method	Stratified Miettinen and Nurminen method
Parameter estimate	Difference in Percentages
Point estimate	-18.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-32
upper limit	-4.3

Notes:

[2] - One-sided p-value for testing. H0: difference in % = 0 versus H1: difference in % > 0.

Secondary: Progression-free survival of Pembrolizumab + Chemotherapy + Epacadostat versus Pembrolizumab + Chemotherapy + Placebo

End point title	Progression-free survival of Pembrolizumab + Chemotherapy + Epacadostat versus Pembrolizumab + Chemotherapy + Placebo[3]

End point description:

Defined as the time from randomization to the first documented progressive disease (PD) per Response Evaluation Criteria in Solid Tumors (RECIST) v1.1 or death due to any cause, whichever occurs first.

End point type	Secondary

End point timeframe:

Up to 24 months

Notes:

[3] - 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: No statistical analysis for this endpoint.

End point values	Pembrolizumab + Chemotherapy + Epacadostat	Pembrolizumab + Chemotherapy + Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	91	87		
Units: months				
median (confidence interval 95%)	8.0 (4.2 to 10.2)	8.2 (6.0 to 999999)		

Statistical analyses

Statistical analysis title	Regression, Cox
Comparison groups	Pembrolizumab + Chemotherapy + Epacadostat v Pembrolizumab + Chemotherapy + Placebo

Number of subjects included in analysis	178
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.94305 [4]
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	1.47
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.91
upper limit	2.36

Notes:

[4] - One-sided p-value based on log-rank test stratified by TPS (<50% vs >=50%) and predominant histology (squamous vs non-squamous), because of small sample size, the strata 'TPS >= 50% Non-squamous' and 'TPS >= 50% Squamous' were combined into one.

Secondary: Overall survival of Pembrolizumab + Chemotherapy + Epacadostat versus Pembrolizumab + Chemotherapy + Placebo

End point title	Overall survival of Pembrolizumab + Chemotherapy + Epacadostat versus Pembrolizumab + Chemotherapy + Placebo[5]

End point description:

Defined as the time from randomization to death due to any cause.

End point type	Secondary

End point timeframe:

Up to 24 months

Notes:

[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: No statistical analysis for this endpoint.

End point values	Pembrolizumab + Chemotherapy + Epacadostat	Pembrolizumab + Chemotherapy + Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	91	87		
Units: months				
median (confidence interval 95%)	9.9999 (0.9999 to 99.999)	9.9999 (0.99999 to 99.9999)		

Statistical analyses

Statistical analysis title	Regression, Cox
Comparison groups	Pembrolizumab + Chemotherapy + Epacadostat v Pembrolizumab + Chemotherapy + Placebo

Number of subjects included in analysis	178
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.96272 [6]
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	1.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.93
upper limit	3.9

Notes:

[6] - One-sided p-value based on log-rank test stratified by PD-L1 TPS (<50% vs >=50%) and predominant tumor histology (squamous vs non-squamous), because of small sample size, the strata (<50% vs >=50%) were combined into one stratum.

Secondary: Duration of response of Pembrolizumab + Chemotherapy + Epacadostat versus Pembrolizumab + Chemotherapy + Placebo

End point title	Duration of response of Pembrolizumab + Chemotherapy + Epacadostat versus Pembrolizumab + Chemotherapy + Placebo[7]

End point description:

Defined as the time from the earliest date of qualifying response until earliest date of disease progression, per RECIST v1.1, or death from any cause, whichever comes first.

End point type	Secondary

End point timeframe:

Up to 24 months

Notes:

[7] - 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: No statistical analysis for this endpoint.

End point values	Pembrolizumab + Chemotherapy + Epacadostat	Pembrolizumab + Chemotherapy + Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	91	87		
Units: months				
median (confidence interval 95%)	2.2222 (1.1 to 7.0)	7.0 (1.2 to 8.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Safety and tolerability of Pembrolizumab + Chemotherapy + Epacadostat versus Pembrolizumab + Chemotherapy + Placebo as measured by the number of participants experiencing adverse events (AEs)

End point title	Safety and tolerability of Pembrolizumab + Chemotherapy + Epacadostat versus Pembrolizumab + Chemotherapy + Placebo as measured by the number of participants experiencing adverse events (AEs)[8]

End point description:

An AE is defined as any untoward medical occurrence in a participant or clinical study participant, temporally associated with the use of study treatment, whether or not considered related to the study treatment.

End point type	Secondary

End point timeframe:

Up to 25 months

Notes:

[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: No statistical analysis for this endpoint.

End point values	Pembrolizumab + Chemotherapy + Epacadostat	Pembrolizumab + Chemotherapy + Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	90	86		
Units: number of participants	89	82		

Statistical analyses

No statistical analyses for this end point

Secondary: Safety and tolerability of Pembrolizumab + Chemotherapy + Epacadostat versus Pembrolizumab + Chemotherapy + Placebo as measured by the number of participants discontinuing study drug due to AEs

End point title	Safety and tolerability of Pembrolizumab + Chemotherapy + Epacadostat versus Pembrolizumab + Chemotherapy + Placebo as measured by the number of participants discontinuing study drug due to AEs[9]

End point description:

An AE is defined as any untoward medical occurrence in a participant or clinical study participant, temporally associated with the use of any study drug, whether or not considered related to the study drug.

End point type	Secondary

End point timeframe:

Up to 25 months

Notes:

[9] - 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: No statistical analysis for this endpoint.

End point values	Pembrolizumab + Chemotherapy + Epacadostat	Pembrolizumab + Chemotherapy + Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	90	86		
Units: Number of Participants	37	35		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Up to 25 months	
Adverse event reporting additional description:	
AE additional description	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	16

Reporting groups	
Reporting group title	Pembrolizumab + Chemotherapy + Epacadostat
Reporting group description:	
Participant received pembrolizumab 200 mg intravenous (IV) infusion, every 3 weeks (Q3W) on Day 1 of each 21 day cycle for up to 35 cycles + epacadostat 100 mg tablets, orally, twice daily (BID) in each 21 day cycle for up to 35 cycles + platinum-doublet chemotherapy (pemetrexed 500 mg/m^2 IV infusion, Q3W + cisplatin 75 mg/m^2 IV infusion, Q3W or carboplatin 5-6 mg/mL/min IV infusion Q3W for 4 cycles followed by pemetrexed maintenance; or paclitaxel 200 mg /m^2 IV infusion, Q3W + carboplatin 5-6 mg/mL/min IV infusion Q3W for 4 cycles).	
Reporting group title	Pembrolizumab + Chemotherapy + Placebo
Reporting group description:	
Participant received pembrolizumab 200 mg IV infusion, Q3W on Day 1 of each 21 day cycle for up to 35 cycles + epacadostat matching placebo tablets, orally, BID in each 21 day cycle for up to 35 cycles + platinum-doublet chemotherapy (pemetrexed 500 mg/m^2 IV infusion, Q3W + cisplatin 75 mg/m^2 IV infusion, Q3W or carboplatin 5-6 mg/mL/min IV infusion Q3W for 4 cycles followed by pemetrexed maintenance; or paclitaxel 200 mg /m^2 IV infusion, Q3W + carboplatin 5-6 mg/mL/min IV infusion Q3W for 4 cycles).	
Reporting group title	Pembrolizumab + Epacadostat
Reporting group description:	
Participant received pembrolizumab 200 mg IV infusion, Q3W on Day 1 of each 21 day cycle for up to 35 cycles + epacadostat 100 mg tablets, orally, BID in each 21 day cycle for up to 35 cycles.	
Reporting group title	Total
Reporting group description:	
Total	

Serious adverse events	Pembrolizumab + Chemotherapy + Epacadostat	Pembrolizumab + Chemotherapy + Placebo	Pembrolizumab + Epacadostat
Total subjects affected by serious adverse events			
subjects affected / exposed	47 / 90 (52.22%)	41 / 86 (47.67%)	20 / 52 (38.46%)
number of deaths (all causes)	38	35	26
number of deaths resulting from adverse events	12	6	10
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cancer pain			

subjects affected / exposed	0 / 90 (0.00%)	1 / 86 (1.16%)	0 / 52 (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
Hypopharyngeal neoplasm			
subjects affected / exposed	0 / 90 (0.00%)	1 / 86 (1.16%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Malignant neoplasm progression			
subjects affected / exposed	5 / 90 (5.56%)	2 / 86 (2.33%)	8 / 52 (15.38%)
occurrences causally related to treatment / all	0 / 5	0 / 2	0 / 8
deaths causally related to treatment / all	0 / 4	0 / 0	0 / 5
Malignant pleural effusion			
subjects affected / exposed	0 / 90 (0.00%)	1 / 86 (1.16%)	0 / 52 (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
Pancreatic carcinoma			
subjects affected / exposed	1 / 90 (1.11%)	0 / 86 (0.00%)	0 / 52 (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
Paraneoplastic syndrome			
subjects affected / exposed	1 / 90 (1.11%)	0 / 86 (0.00%)	0 / 52 (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
Prostate cancer			
subjects affected / exposed	0 / 90 (0.00%)	1 / 86 (1.16%)	0 / 52 (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			
Embolism			
subjects affected / exposed	1 / 90 (1.11%)	0 / 86 (0.00%)	0 / 52 (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
Hypertension			

subjects affected / exposed	1 / 90 (1.11%)	0 / 86 (0.00%)	0 / 52 (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
Peripheral ischaemia			
subjects affected / exposed	0 / 90 (0.00%)	1 / 86 (1.16%)	0 / 52 (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
Superior vena cava syndrome			
subjects affected / exposed	1 / 90 (1.11%)	0 / 86 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Breakthrough pain			
subjects affected / exposed	1 / 90 (1.11%)	0 / 86 (0.00%)	0 / 52 (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 / 90 (0.00%)	1 / 86 (1.16%)	0 / 52 (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
Death			
subjects affected / exposed	0 / 90 (0.00%)	0 / 86 (0.00%)	2 / 52 (3.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 2
General physical health deterioration			
subjects affected / exposed	0 / 90 (0.00%)	1 / 86 (1.16%)	0 / 52 (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
Infusion site extravasation			
subjects affected / exposed	1 / 90 (1.11%)	0 / 86 (0.00%)	0 / 52 (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
Malaise			

subjects affected / exposed	0 / 90 (0.00%)	1 / 86 (1.16%)	0 / 52 (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
Mucosal inflammation			
subjects affected / exposed	0 / 90 (0.00%)	1 / 86 (1.16%)	0 / 52 (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	2 / 90 (2.22%)	0 / 86 (0.00%)	0 / 52 (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
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 90 (0.00%)	1 / 86 (1.16%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 90 (0.00%)	1 / 86 (1.16%)	0 / 52 (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
Cough			
subjects affected / exposed	0 / 90 (0.00%)	1 / 86 (1.16%)	0 / 52 (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
Dyspnoea			
subjects affected / exposed	0 / 90 (0.00%)	1 / 86 (1.16%)	0 / 52 (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
Haemoptysis			
subjects affected / exposed	2 / 90 (2.22%)	1 / 86 (1.16%)	0 / 52 (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

Haemothorax			
subjects affected / exposed	1 / 90 (1.11%)	0 / 86 (0.00%)	0 / 52 (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
Hypoxia			
subjects affected / exposed	1 / 90 (1.11%)	0 / 86 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion			
subjects affected / exposed	2 / 90 (2.22%)	1 / 86 (1.16%)	2 / 52 (3.85%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonitis			
subjects affected / exposed	1 / 90 (1.11%)	3 / 86 (3.49%)	0 / 52 (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
Pulmonary embolism			
subjects affected / exposed	1 / 90 (1.11%)	1 / 86 (1.16%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary oedema			
subjects affected / exposed	1 / 90 (1.11%)	0 / 86 (0.00%)	0 / 52 (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
Respiratory failure			
subjects affected / exposed	1 / 90 (1.11%)	1 / 86 (1.16%)	0 / 52 (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
Psychiatric disorders			
Agitation			
subjects affected / exposed	0 / 90 (0.00%)	1 / 86 (1.16%)	0 / 52 (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
Confusional state			

subjects affected / exposed	0 / 90 (0.00%)	1 / 86 (1.16%)	0 / 52 (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
Hallucination			
subjects affected / exposed	0 / 90 (0.00%)	0 / 86 (0.00%)	1 / 52 (1.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 90 (1.11%)	0 / 86 (0.00%)	0 / 52 (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
Liver function test increased			
subjects affected / exposed	1 / 90 (1.11%)	0 / 86 (0.00%)	0 / 52 (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
Pancreatic enzymes increased			
subjects affected / exposed	1 / 90 (1.11%)	0 / 86 (0.00%)	0 / 52 (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
Platelet count decreased			
subjects affected / exposed	0 / 90 (0.00%)	1 / 86 (1.16%)	0 / 52 (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
Injury, poisoning and procedural complications			
Femoral neck fracture			
subjects affected / exposed	0 / 90 (0.00%)	1 / 86 (1.16%)	0 / 52 (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
Hip fracture			
subjects affected / exposed	0 / 90 (0.00%)	1 / 86 (1.16%)	0 / 52 (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

Humerus fracture			
subjects affected / exposed	0 / 90 (0.00%)	0 / 86 (0.00%)	1 / 52 (1.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Radiation necrosis			
subjects affected / exposed	1 / 90 (1.11%)	1 / 86 (1.16%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal compression fracture			
subjects affected / exposed	1 / 90 (1.11%)	0 / 86 (0.00%)	0 / 52 (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
Subdural haemorrhage			
subjects affected / exposed	1 / 90 (1.11%)	0 / 86 (0.00%)	0 / 52 (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
Cardiac disorders			
Acute coronary syndrome			
subjects affected / exposed	0 / 90 (0.00%)	1 / 86 (1.16%)	1 / 52 (1.92%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute myocardial infarction			
subjects affected / exposed	0 / 90 (0.00%)	1 / 86 (1.16%)	0 / 52 (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 fibrillation			
subjects affected / exposed	1 / 90 (1.11%)	2 / 86 (2.33%)	0 / 52 (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
Atrioventricular block complete			
subjects affected / exposed	1 / 90 (1.11%)	0 / 86 (0.00%)	0 / 52 (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
Cardiac arrest			

subjects affected / exposed	0 / 90 (0.00%)	2 / 86 (2.33%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Cardiac failure acute			
subjects affected / exposed	1 / 90 (1.11%)	0 / 86 (0.00%)	0 / 52 (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
Cardio-respiratory arrest			
subjects affected / exposed	1 / 90 (1.11%)	0 / 86 (0.00%)	0 / 52 (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
Myocardial infarction			
subjects affected / exposed	1 / 90 (1.11%)	0 / 86 (0.00%)	1 / 52 (1.92%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
Pericardial effusion			
subjects affected / exposed	0 / 90 (0.00%)	0 / 86 (0.00%)	1 / 52 (1.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	2 / 90 (2.22%)	1 / 86 (1.16%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Embolic stroke			
subjects affected / exposed	1 / 90 (1.11%)	0 / 86 (0.00%)	0 / 52 (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
Encephalopathy			
subjects affected / exposed	0 / 90 (0.00%)	1 / 86 (1.16%)	0 / 52 (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
Peripheral sensory neuropathy			

subjects affected / exposed	0 / 90 (0.00%)	1 / 86 (1.16%)	0 / 52 (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
Sciatica			
subjects affected / exposed	0 / 90 (0.00%)	1 / 86 (1.16%)	0 / 52 (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
Syncope			
subjects affected / exposed	0 / 90 (0.00%)	1 / 86 (1.16%)	1 / 52 (1.92%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient ischaemic attack			
subjects affected / exposed	1 / 90 (1.11%)	0 / 86 (0.00%)	0 / 52 (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
Vocal cord paralysis			
subjects affected / exposed	0 / 90 (0.00%)	0 / 86 (0.00%)	1 / 52 (1.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 90 (1.11%)	1 / 86 (1.16%)	0 / 52 (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
Febrile neutropenia			
subjects affected / exposed	5 / 90 (5.56%)	0 / 86 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 5	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymphadenopathy			
subjects affected / exposed	1 / 90 (1.11%)	0 / 86 (0.00%)	0 / 52 (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
Neutropenia			

subjects affected / exposed	2 / 90 (2.22%)	0 / 86 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancytopenia			
subjects affected / exposed	1 / 90 (1.11%)	0 / 86 (0.00%)	0 / 52 (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
Thrombocytopenia			
subjects affected / exposed	0 / 90 (0.00%)	1 / 86 (1.16%)	0 / 52 (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 upper			
subjects affected / exposed	0 / 90 (0.00%)	1 / 86 (1.16%)	0 / 52 (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
Colitis			
subjects affected / exposed	0 / 90 (0.00%)	2 / 86 (2.33%)	1 / 52 (1.92%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Constipation			
subjects affected / exposed	0 / 90 (0.00%)	1 / 86 (1.16%)	0 / 52 (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	2 / 90 (2.22%)	2 / 86 (2.33%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal toxicity			
subjects affected / exposed	0 / 90 (0.00%)	0 / 86 (0.00%)	1 / 52 (1.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Odynophagia			

subjects affected / exposed	1 / 90 (1.11%)	0 / 86 (0.00%)	0 / 52 (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
Pancreatitis acute			
subjects affected / exposed	1 / 90 (1.11%)	1 / 86 (1.16%)	0 / 52 (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
Stomatitis			
subjects affected / exposed	1 / 90 (1.11%)	1 / 86 (1.16%)	0 / 52 (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
Vomiting			
subjects affected / exposed	2 / 90 (2.22%)	0 / 86 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Autoimmune hepatitis			
subjects affected / exposed	1 / 90 (1.11%)	0 / 86 (0.00%)	0 / 52 (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
Cholecystitis			
subjects affected / exposed	1 / 90 (1.11%)	0 / 86 (0.00%)	0 / 52 (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
Cholecystitis acute			
subjects affected / exposed	0 / 90 (0.00%)	1 / 86 (1.16%)	0 / 52 (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
Gallbladder rupture			
subjects affected / exposed	1 / 90 (1.11%)	0 / 86 (0.00%)	0 / 52 (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
Hepatotoxicity			

subjects affected / exposed	1 / 90 (1.11%)	0 / 86 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Exfoliative rash			
subjects affected / exposed	1 / 90 (1.11%)	0 / 86 (0.00%)	0 / 52 (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
Purpura			
subjects affected / exposed	0 / 90 (0.00%)	1 / 86 (1.16%)	0 / 52 (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
Rash			
subjects affected / exposed	1 / 90 (1.11%)	0 / 86 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin ulcer			
subjects affected / exposed	1 / 90 (1.11%)	0 / 86 (0.00%)	0 / 52 (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
Stevens-Johnson syndrome			
subjects affected / exposed	0 / 90 (0.00%)	1 / 86 (1.16%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	2 / 90 (2.22%)	0 / 86 (0.00%)	0 / 52 (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
Endocrine disorders			
Hyperthyroidism			
subjects affected / exposed	0 / 90 (0.00%)	0 / 86 (0.00%)	1 / 52 (1.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Musculoskeletal and connective tissue disorders			
Arthropathy			
subjects affected / exposed	1 / 90 (1.11%)	0 / 86 (0.00%)	0 / 52 (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
Myalgia			
subjects affected / exposed	0 / 90 (0.00%)	1 / 86 (1.16%)	0 / 52 (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
Pain in extremity			
subjects affected / exposed	1 / 90 (1.11%)	0 / 86 (0.00%)	0 / 52 (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
Rhabdomyolysis			
subjects affected / exposed	1 / 90 (1.11%)	0 / 86 (0.00%)	0 / 52 (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
Infections and infestations			
Bronchitis			
subjects affected / exposed	3 / 90 (3.33%)	1 / 86 (1.16%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	1 / 90 (1.11%)	0 / 86 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Encephalitis			
subjects affected / exposed	1 / 90 (1.11%)	0 / 86 (0.00%)	0 / 52 (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
Gastroenteritis			
subjects affected / exposed	1 / 90 (1.11%)	0 / 86 (0.00%)	0 / 52 (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

Gingivitis			
subjects affected / exposed	1 / 90 (1.11%)	0 / 86 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes zoster			
subjects affected / exposed	0 / 90 (0.00%)	1 / 86 (1.16%)	0 / 52 (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
Lower respiratory tract infection			
subjects affected / exposed	3 / 90 (3.33%)	1 / 86 (1.16%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ophthalmic herpes zoster			
subjects affected / exposed	1 / 90 (1.11%)	0 / 86 (0.00%)	0 / 52 (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
Pneumocystis jirovecii pneumonia			
subjects affected / exposed	0 / 90 (0.00%)	0 / 86 (0.00%)	1 / 52 (1.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Pneumonia			
subjects affected / exposed	5 / 90 (5.56%)	12 / 86 (13.95%)	4 / 52 (7.69%)
occurrences causally related to treatment / all	0 / 5	0 / 12	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Sepsis			
subjects affected / exposed	3 / 90 (3.33%)	0 / 86 (0.00%)	1 / 52 (1.92%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 2	0 / 0	0 / 1
Urinary tract infection			
subjects affected / exposed	1 / 90 (1.11%)	1 / 86 (1.16%)	0 / 52 (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
Urosepsis			

subjects affected / exposed	0 / 90 (0.00%)	1 / 86 (1.16%)	0 / 52 (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 device infection			
subjects affected / exposed	1 / 90 (1.11%)	0 / 86 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 90 (0.00%)	1 / 86 (1.16%)	1 / 52 (1.92%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dehydration			
subjects affected / exposed	2 / 90 (2.22%)	0 / 86 (0.00%)	1 / 52 (1.92%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetes mellitus			
subjects affected / exposed	0 / 90 (0.00%)	1 / 86 (1.16%)	0 / 52 (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
Diabetic ketoacidosis			
subjects affected / exposed	1 / 90 (1.11%)	0 / 86 (0.00%)	0 / 52 (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
Hyperglycaemia			
subjects affected / exposed	0 / 90 (0.00%)	0 / 86 (0.00%)	1 / 52 (1.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperkalaemia			
subjects affected / exposed	0 / 90 (0.00%)	1 / 86 (1.16%)	0 / 52 (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 / 90 (0.00%)	0 / 86 (0.00%)	1 / 52 (1.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Total		
Total subjects affected by serious adverse events			
subjects affected / exposed	108 / 228 (47.37%)		
number of deaths (all causes)	99		
number of deaths resulting from adverse events	28		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cancer pain			
subjects affected / exposed	1 / 228 (0.44%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hypopharyngeal neoplasm			
subjects affected / exposed	1 / 228 (0.44%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Malignant neoplasm progression			
subjects affected / exposed	15 / 228 (6.58%)		
occurrences causally related to treatment / all	0 / 15		
deaths causally related to treatment / all	0 / 9		
Malignant pleural effusion			
subjects affected / exposed	1 / 228 (0.44%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pancreatic carcinoma			
subjects affected / exposed	1 / 228 (0.44%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Paraneoplastic syndrome			
subjects affected / exposed	1 / 228 (0.44%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Prostate cancer				
subjects affected / exposed	1 / 228 (0.44%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Vascular disorders				
Embolism				
subjects affected / exposed	1 / 228 (0.44%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hypertension				
subjects affected / exposed	1 / 228 (0.44%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Peripheral ischaemia				
subjects affected / exposed	1 / 228 (0.44%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Superior vena cava syndrome				
subjects affected / exposed	1 / 228 (0.44%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
General disorders and administration site conditions				
Breakthrough pain				
subjects affected / exposed	1 / 228 (0.44%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Chest pain				
subjects affected / exposed	1 / 228 (0.44%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Death				
subjects affected / exposed	2 / 228 (0.88%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 2			

General physical health deterioration				
subjects affected / exposed	1 / 228 (0.44%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Infusion site extravasation				
subjects affected / exposed	1 / 228 (0.44%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Malaise				
subjects affected / exposed	1 / 228 (0.44%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Mucosal inflammation				
subjects affected / exposed	1 / 228 (0.44%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pyrexia				
subjects affected / exposed	2 / 228 (0.88%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Immune system disorders				
Hypersensitivity				
subjects affected / exposed	1 / 228 (0.44%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Chronic obstructive pulmonary disease				
subjects affected / exposed	1 / 228 (0.44%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cough				

subjects affected / exposed	1 / 228 (0.44%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Dyspnoea				
subjects affected / exposed	1 / 228 (0.44%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Haemoptysis				
subjects affected / exposed	3 / 228 (1.32%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 1			
Haemothorax				
subjects affected / exposed	1 / 228 (0.44%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hypoxia				
subjects affected / exposed	1 / 228 (0.44%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pleural effusion				
subjects affected / exposed	5 / 228 (2.19%)			
occurrences causally related to treatment / all	0 / 5			
deaths causally related to treatment / all	0 / 0			
Pneumonitis				
subjects affected / exposed	4 / 228 (1.75%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 2			
Pulmonary embolism				
subjects affected / exposed	2 / 228 (0.88%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Pulmonary oedema				

subjects affected / exposed	1 / 228 (0.44%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory failure				
subjects affected / exposed	2 / 228 (0.88%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 2			
Psychiatric disorders				
Agitation				
subjects affected / exposed	1 / 228 (0.44%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Confusional state				
subjects affected / exposed	1 / 228 (0.44%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hallucination				
subjects affected / exposed	1 / 228 (0.44%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Investigations				
Alanine aminotransferase increased				
subjects affected / exposed	1 / 228 (0.44%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Liver function test increased				
subjects affected / exposed	1 / 228 (0.44%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pancreatic enzymes increased				
subjects affected / exposed	1 / 228 (0.44%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Platelet count decreased				

subjects affected / exposed	1 / 228 (0.44%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Femoral neck fracture			
subjects affected / exposed	1 / 228 (0.44%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hip fracture			
subjects affected / exposed	1 / 228 (0.44%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Humerus fracture			
subjects affected / exposed	1 / 228 (0.44%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Radiation necrosis			
subjects affected / exposed	2 / 228 (0.88%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Spinal compression fracture			
subjects affected / exposed	1 / 228 (0.44%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Subdural haemorrhage			
subjects affected / exposed	1 / 228 (0.44%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Acute coronary syndrome			
subjects affected / exposed	2 / 228 (0.88%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		

Acute myocardial infarction			
subjects affected / exposed	1 / 228 (0.44%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Atrial fibrillation			
subjects affected / exposed	3 / 228 (1.32%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Atrioventricular block complete			
subjects affected / exposed	1 / 228 (0.44%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac arrest			
subjects affected / exposed	2 / 228 (0.88%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 1		
Cardiac failure acute			
subjects affected / exposed	1 / 228 (0.44%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardio-respiratory arrest			
subjects affected / exposed	1 / 228 (0.44%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Myocardial infarction			
subjects affected / exposed	2 / 228 (0.88%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 2		
Pericardial effusion			
subjects affected / exposed	1 / 228 (0.44%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			

Cerebrovascular accident			
subjects affected / exposed	3 / 228 (1.32%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Embolic stroke			
subjects affected / exposed	1 / 228 (0.44%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Encephalopathy			
subjects affected / exposed	1 / 228 (0.44%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Peripheral sensory neuropathy			
subjects affected / exposed	1 / 228 (0.44%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Sciatica			
subjects affected / exposed	1 / 228 (0.44%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Syncope			
subjects affected / exposed	2 / 228 (0.88%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Transient ischaemic attack			
subjects affected / exposed	1 / 228 (0.44%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vocal cord paralysis			
subjects affected / exposed	1 / 228 (0.44%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			

Anaemia				
subjects affected / exposed	2 / 228 (0.88%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Febrile neutropenia				
subjects affected / exposed	5 / 228 (2.19%)			
occurrences causally related to treatment / all	0 / 5			
deaths causally related to treatment / all	0 / 0			
Lymphadenopathy				
subjects affected / exposed	1 / 228 (0.44%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Neutropenia				
subjects affected / exposed	2 / 228 (0.88%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Pancytopenia				
subjects affected / exposed	1 / 228 (0.44%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Thrombocytopenia				
subjects affected / exposed	1 / 228 (0.44%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
Abdominal pain upper				
subjects affected / exposed	1 / 228 (0.44%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Colitis				
subjects affected / exposed	3 / 228 (1.32%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Constipation				

subjects affected / exposed	1 / 228 (0.44%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Diarrhoea				
subjects affected / exposed	4 / 228 (1.75%)			
occurrences causally related to treatment / all	0 / 5			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal toxicity				
subjects affected / exposed	1 / 228 (0.44%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Odynophagia				
subjects affected / exposed	1 / 228 (0.44%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pancreatitis acute				
subjects affected / exposed	2 / 228 (0.88%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Stomatitis				
subjects affected / exposed	2 / 228 (0.88%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Vomiting				
subjects affected / exposed	2 / 228 (0.88%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Hepatobiliary disorders				
Autoimmune hepatitis				
subjects affected / exposed	1 / 228 (0.44%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cholecystitis				

subjects affected / exposed	1 / 228 (0.44%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cholecystitis acute				
subjects affected / exposed	1 / 228 (0.44%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gallbladder rupture				
subjects affected / exposed	1 / 228 (0.44%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hepatotoxicity				
subjects affected / exposed	1 / 228 (0.44%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Skin and subcutaneous tissue disorders				
Exfoliative rash				
subjects affected / exposed	1 / 228 (0.44%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Purpura				
subjects affected / exposed	1 / 228 (0.44%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Rash				
subjects affected / exposed	1 / 228 (0.44%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Skin ulcer				
subjects affected / exposed	1 / 228 (0.44%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Stevens-Johnson syndrome				

subjects affected / exposed	1 / 228 (0.44%)		
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	2 / 228 (0.88%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Endocrine disorders			
Hyperthyroidism			
subjects affected / exposed	1 / 228 (0.44%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Arthropathy			
subjects affected / exposed	1 / 228 (0.44%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Myalgia			
subjects affected / exposed	1 / 228 (0.44%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pain in extremity			
subjects affected / exposed	1 / 228 (0.44%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Rhabdomyolysis			
subjects affected / exposed	1 / 228 (0.44%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Bronchitis			

subjects affected / exposed	4 / 228 (1.75%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 0			
Cellulitis				
subjects affected / exposed	1 / 228 (0.44%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Encephalitis				
subjects affected / exposed	1 / 228 (0.44%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis				
subjects affected / exposed	1 / 228 (0.44%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gingivitis				
subjects affected / exposed	1 / 228 (0.44%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Herpes zoster				
subjects affected / exposed	1 / 228 (0.44%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Lower respiratory tract infection				
subjects affected / exposed	4 / 228 (1.75%)			
occurrences causally related to treatment / all	0 / 5			
deaths causally related to treatment / all	0 / 0			
Ophthalmic herpes zoster				
subjects affected / exposed	1 / 228 (0.44%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumocystis jirovecii pneumonia				

subjects affected / exposed	1 / 228 (0.44%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Pneumonia				
subjects affected / exposed	21 / 228 (9.21%)			
occurrences causally related to treatment / all	0 / 21			
deaths causally related to treatment / all	0 / 1			
Sepsis				
subjects affected / exposed	4 / 228 (1.75%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 3			
Urinary tract infection				
subjects affected / exposed	2 / 228 (0.88%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Urosepsis				
subjects affected / exposed	1 / 228 (0.44%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Vascular device infection				
subjects affected / exposed	1 / 228 (0.44%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Metabolism and nutrition disorders				
Decreased appetite				
subjects affected / exposed	2 / 228 (0.88%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Dehydration				
subjects affected / exposed	3 / 228 (1.32%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Diabetes mellitus				

subjects affected / exposed	1 / 228 (0.44%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Diabetic ketoacidosis			
subjects affected / exposed	1 / 228 (0.44%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hyperglycaemia			
subjects affected / exposed	1 / 228 (0.44%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hyperkalaemia			
subjects affected / exposed	1 / 228 (0.44%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hyponatraemia			
subjects affected / exposed	1 / 228 (0.44%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Pembrolizumab + Chemotherapy + Epacadostat	Pembrolizumab + Chemotherapy + Placebo	Pembrolizumab + Epacadostat
Total subjects affected by non-serious adverse events			
subjects affected / exposed	87 / 90 (96.67%)	81 / 86 (94.19%)	51 / 52 (98.08%)
Vascular disorders			
Hypertension			
subjects affected / exposed	5 / 90 (5.56%)	3 / 86 (3.49%)	0 / 52 (0.00%)
occurrences (all)	7	4	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	12 / 90 (13.33%)	18 / 86 (20.93%)	6 / 52 (11.54%)
occurrences (all)	14	24	9
Chest pain			

subjects affected / exposed	3 / 90 (3.33%)	13 / 86 (15.12%)	10 / 52 (19.23%)
occurrences (all)	3	13	11
Fatigue			
subjects affected / exposed	28 / 90 (31.11%)	25 / 86 (29.07%)	14 / 52 (26.92%)
occurrences (all)	40	32	16
Mucosal inflammation			
subjects affected / exposed	5 / 90 (5.56%)	7 / 86 (8.14%)	0 / 52 (0.00%)
occurrences (all)	7	8	0
Oedema peripheral			
subjects affected / exposed	14 / 90 (15.56%)	10 / 86 (11.63%)	4 / 52 (7.69%)
occurrences (all)	20	11	4
Peripheral swelling			
subjects affected / exposed	6 / 90 (6.67%)	2 / 86 (2.33%)	1 / 52 (1.92%)
occurrences (all)	9	3	1
Pyrexia			
subjects affected / exposed	15 / 90 (16.67%)	10 / 86 (11.63%)	9 / 52 (17.31%)
occurrences (all)	21	12	13
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	10 / 90 (11.11%)	11 / 86 (12.79%)	12 / 52 (23.08%)
occurrences (all)	10	13	14
Dyspnoea			
subjects affected / exposed	12 / 90 (13.33%)	11 / 86 (12.79%)	7 / 52 (13.46%)
occurrences (all)	14	11	7
Epistaxis			
subjects affected / exposed	7 / 90 (7.78%)	6 / 86 (6.98%)	1 / 52 (1.92%)
occurrences (all)	7	8	1
Haemoptysis			
subjects affected / exposed	4 / 90 (4.44%)	7 / 86 (8.14%)	3 / 52 (5.77%)
occurrences (all)	4	9	3
Oropharyngeal pain			
subjects affected / exposed	5 / 90 (5.56%)	2 / 86 (2.33%)	1 / 52 (1.92%)
occurrences (all)	5	2	1
Pneumonitis			

subjects affected / exposed	2 / 90 (2.22%)	6 / 86 (6.98%)	0 / 52 (0.00%)
occurrences (all)	2	7	0
Productive cough			
subjects affected / exposed	5 / 90 (5.56%)	1 / 86 (1.16%)	4 / 52 (7.69%)
occurrences (all)	5	1	4
Rhinorrhoea			
subjects affected / exposed	10 / 90 (11.11%)	0 / 86 (0.00%)	2 / 52 (3.85%)
occurrences (all)	12	0	2
Psychiatric disorders			
Anxiety			
subjects affected / exposed	3 / 90 (3.33%)	5 / 86 (5.81%)	2 / 52 (3.85%)
occurrences (all)	3	5	2
Insomnia			
subjects affected / exposed	16 / 90 (17.78%)	7 / 86 (8.14%)	2 / 52 (3.85%)
occurrences (all)	16	7	2
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	15 / 90 (16.67%)	10 / 86 (11.63%)	1 / 52 (1.92%)
occurrences (all)	20	12	3
Amylase increased			
subjects affected / exposed	10 / 90 (11.11%)	10 / 86 (11.63%)	7 / 52 (13.46%)
occurrences (all)	14	10	8
Aspartate aminotransferase increased			
subjects affected / exposed	15 / 90 (16.67%)	8 / 86 (9.30%)	3 / 52 (5.77%)
occurrences (all)	22	10	5
Blood alkaline phosphatase increased			
subjects affected / exposed	7 / 90 (7.78%)	3 / 86 (3.49%)	2 / 52 (3.85%)
occurrences (all)	7	4	2
Blood creatinine increased			
subjects affected / exposed	7 / 90 (7.78%)	7 / 86 (8.14%)	4 / 52 (7.69%)
occurrences (all)	8	11	4
Gamma-glutamyltransferase increased			
subjects affected / exposed	5 / 90 (5.56%)	7 / 86 (8.14%)	3 / 52 (5.77%)
occurrences (all)	5	12	3
Lipase increased			

subjects affected / exposed	7 / 90 (7.78%)	6 / 86 (6.98%)	5 / 52 (9.62%)
occurrences (all)	9	7	5
Neutrophil count decreased			
subjects affected / exposed	4 / 90 (4.44%)	14 / 86 (16.28%)	0 / 52 (0.00%)
occurrences (all)	8	20	0
Platelet count decreased			
subjects affected / exposed	5 / 90 (5.56%)	9 / 86 (10.47%)	0 / 52 (0.00%)
occurrences (all)	9	12	0
Weight decreased			
subjects affected / exposed	10 / 90 (11.11%)	8 / 86 (9.30%)	7 / 52 (13.46%)
occurrences (all)	10	9	7
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	3 / 90 (3.33%)	5 / 86 (5.81%)	1 / 52 (1.92%)
occurrences (all)	3	6	1
Nervous system disorders			
Dizziness			
subjects affected / exposed	16 / 90 (17.78%)	13 / 86 (15.12%)	5 / 52 (9.62%)
occurrences (all)	17	17	7
Dysgeusia			
subjects affected / exposed	8 / 90 (8.89%)	5 / 86 (5.81%)	0 / 52 (0.00%)
occurrences (all)	9	6	0
Headache			
subjects affected / exposed	14 / 90 (15.56%)	11 / 86 (12.79%)	5 / 52 (9.62%)
occurrences (all)	18	13	7
Hypoaesthesia			
subjects affected / exposed	7 / 90 (7.78%)	7 / 86 (8.14%)	0 / 52 (0.00%)
occurrences (all)	7	8	0
Neuropathy peripheral			
subjects affected / exposed	14 / 90 (15.56%)	10 / 86 (11.63%)	1 / 52 (1.92%)
occurrences (all)	14	10	2
Paraesthesia			
subjects affected / exposed	6 / 90 (6.67%)	1 / 86 (1.16%)	0 / 52 (0.00%)
occurrences (all)	6	1	0
Blood and lymphatic system disorders			

Anaemia			
subjects affected / exposed	24 / 90 (26.67%)	37 / 86 (43.02%)	8 / 52 (15.38%)
occurrences (all)	34	56	11
Leukopenia			
subjects affected / exposed	6 / 90 (6.67%)	4 / 86 (4.65%)	0 / 52 (0.00%)
occurrences (all)	25	7	0
Neutropenia			
subjects affected / exposed	16 / 90 (17.78%)	15 / 86 (17.44%)	2 / 52 (3.85%)
occurrences (all)	24	25	3
Thrombocytopenia			
subjects affected / exposed	9 / 90 (10.00%)	2 / 86 (2.33%)	0 / 52 (0.00%)
occurrences (all)	14	3	0
Eye disorders			
Lacrimation increased			
subjects affected / exposed	11 / 90 (12.22%)	8 / 86 (9.30%)	0 / 52 (0.00%)
occurrences (all)	13	8	0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	6 / 90 (6.67%)	3 / 86 (3.49%)	5 / 52 (9.62%)
occurrences (all)	8	3	5
Abdominal pain upper			
subjects affected / exposed	3 / 90 (3.33%)	7 / 86 (8.14%)	0 / 52 (0.00%)
occurrences (all)	3	8	0
Constipation			
subjects affected / exposed	26 / 90 (28.89%)	23 / 86 (26.74%)	8 / 52 (15.38%)
occurrences (all)	40	35	9
Diarrhoea			
subjects affected / exposed	23 / 90 (25.56%)	23 / 86 (26.74%)	14 / 52 (26.92%)
occurrences (all)	36	35	19
Dry mouth			
subjects affected / exposed	1 / 90 (1.11%)	5 / 86 (5.81%)	0 / 52 (0.00%)
occurrences (all)	1	5	0
Dyspepsia			
subjects affected / exposed	6 / 90 (6.67%)	1 / 86 (1.16%)	3 / 52 (5.77%)
occurrences (all)	11	2	5
Dysphagia			

subjects affected / exposed	5 / 90 (5.56%)	4 / 86 (4.65%)	0 / 52 (0.00%)
occurrences (all)	5	4	0
Nausea			
subjects affected / exposed	38 / 90 (42.22%)	37 / 86 (43.02%)	10 / 52 (19.23%)
occurrences (all)	80	101	13
Vomiting			
subjects affected / exposed	19 / 90 (21.11%)	11 / 86 (12.79%)	6 / 52 (11.54%)
occurrences (all)	29	14	6
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	11 / 90 (12.22%)	16 / 86 (18.60%)	0 / 52 (0.00%)
occurrences (all)	11	16	0
Pruritus			
subjects affected / exposed	12 / 90 (13.33%)	11 / 86 (12.79%)	6 / 52 (11.54%)
occurrences (all)	13	14	11
Rash			
subjects affected / exposed	22 / 90 (24.44%)	18 / 86 (20.93%)	10 / 52 (19.23%)
occurrences (all)	35	25	13
Rash maculo-papular			
subjects affected / exposed	5 / 90 (5.56%)	2 / 86 (2.33%)	0 / 52 (0.00%)
occurrences (all)	5	2	0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	4 / 90 (4.44%)	6 / 86 (6.98%)	0 / 52 (0.00%)
occurrences (all)	4	6	0
Endocrine disorders			
Hyperthyroidism			
subjects affected / exposed	6 / 90 (6.67%)	6 / 86 (6.98%)	3 / 52 (5.77%)
occurrences (all)	8	6	3
Hypothyroidism			
subjects affected / exposed	10 / 90 (11.11%)	9 / 86 (10.47%)	7 / 52 (13.46%)
occurrences (all)	10	9	8
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	14 / 90 (15.56%)	10 / 86 (11.63%)	5 / 52 (9.62%)
occurrences (all)	21	13	5

Back pain			
subjects affected / exposed	14 / 90 (15.56%)	10 / 86 (11.63%)	8 / 52 (15.38%)
occurrences (all)	18	10	9
Bone pain			
subjects affected / exposed	5 / 90 (5.56%)	0 / 86 (0.00%)	3 / 52 (5.77%)
occurrences (all)	8	0	3
Muscular weakness			
subjects affected / exposed	6 / 90 (6.67%)	3 / 86 (3.49%)	2 / 52 (3.85%)
occurrences (all)	6	3	3
Myalgia			
subjects affected / exposed	5 / 90 (5.56%)	3 / 86 (3.49%)	2 / 52 (3.85%)
occurrences (all)	5	3	2
Neck pain			
subjects affected / exposed	5 / 90 (5.56%)	2 / 86 (2.33%)	1 / 52 (1.92%)
occurrences (all)	5	2	1
Pain in extremity			
subjects affected / exposed	11 / 90 (12.22%)	5 / 86 (5.81%)	2 / 52 (3.85%)
occurrences (all)	12	5	3
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	5 / 90 (5.56%)	5 / 86 (5.81%)	3 / 52 (5.77%)
occurrences (all)	8	9	3
Pneumonia			
subjects affected / exposed	7 / 90 (7.78%)	1 / 86 (1.16%)	2 / 52 (3.85%)
occurrences (all)	7	1	2
Upper respiratory tract infection			
subjects affected / exposed	11 / 90 (12.22%)	6 / 86 (6.98%)	1 / 52 (1.92%)
occurrences (all)	14	7	1
Urinary tract infection			
subjects affected / exposed	5 / 90 (5.56%)	9 / 86 (10.47%)	4 / 52 (7.69%)
occurrences (all)	8	10	4
Viral infection			
subjects affected / exposed	5 / 90 (5.56%)	2 / 86 (2.33%)	0 / 52 (0.00%)
occurrences (all)	6	3	0
Metabolism and nutrition disorders			

Decreased appetite			
subjects affected / exposed	19 / 90 (21.11%)	20 / 86 (23.26%)	8 / 52 (15.38%)
occurrences (all)	23	23	11
Dehydration			
subjects affected / exposed	4 / 90 (4.44%)	2 / 86 (2.33%)	3 / 52 (5.77%)
occurrences (all)	5	2	6
Hypercalcaemia			
subjects affected / exposed	5 / 90 (5.56%)	1 / 86 (1.16%)	1 / 52 (1.92%)
occurrences (all)	6	1	1
Hyperglycaemia			
subjects affected / exposed	4 / 90 (4.44%)	6 / 86 (6.98%)	2 / 52 (3.85%)
occurrences (all)	6	6	5
Hypoalbuminaemia			
subjects affected / exposed	1 / 90 (1.11%)	5 / 86 (5.81%)	0 / 52 (0.00%)
occurrences (all)	3	6	0
Hypokalaemia			
subjects affected / exposed	9 / 90 (10.00%)	8 / 86 (9.30%)	1 / 52 (1.92%)
occurrences (all)	13	12	1
Hypomagnesaemia			
subjects affected / exposed	8 / 90 (8.89%)	7 / 86 (8.14%)	1 / 52 (1.92%)
occurrences (all)	12	10	1
Hyponatraemia			
subjects affected / exposed	4 / 90 (4.44%)	6 / 86 (6.98%)	1 / 52 (1.92%)
occurrences (all)	4	11	1

Non-serious adverse events	Total		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	219 / 228 (96.05%)		
Vascular disorders			
Hypertension			
subjects affected / exposed	8 / 228 (3.51%)		
occurrences (all)	11		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	36 / 228 (15.79%)		
occurrences (all)	47		
Chest pain			

subjects affected / exposed	26 / 228 (11.40%)		
occurrences (all)	27		
Fatigue			
subjects affected / exposed	67 / 228 (29.39%)		
occurrences (all)	88		
Mucosal inflammation			
subjects affected / exposed	12 / 228 (5.26%)		
occurrences (all)	15		
Oedema peripheral			
subjects affected / exposed	28 / 228 (12.28%)		
occurrences (all)	35		
Peripheral swelling			
subjects affected / exposed	9 / 228 (3.95%)		
occurrences (all)	13		
Pyrexia			
subjects affected / exposed	34 / 228 (14.91%)		
occurrences (all)	46		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	33 / 228 (14.47%)		
occurrences (all)	37		
Dyspnoea			
subjects affected / exposed	30 / 228 (13.16%)		
occurrences (all)	32		
Epistaxis			
subjects affected / exposed	14 / 228 (6.14%)		
occurrences (all)	16		
Haemoptysis			
subjects affected / exposed	14 / 228 (6.14%)		
occurrences (all)	16		
Oropharyngeal pain			
subjects affected / exposed	8 / 228 (3.51%)		
occurrences (all)	8		
Pneumonitis			

subjects affected / exposed	8 / 228 (3.51%)		
occurrences (all)	9		
Productive cough			
subjects affected / exposed	10 / 228 (4.39%)		
occurrences (all)	10		
Rhinorrhoea			
subjects affected / exposed	12 / 228 (5.26%)		
occurrences (all)	14		
Psychiatric disorders			
Anxiety			
subjects affected / exposed	10 / 228 (4.39%)		
occurrences (all)	10		
Insomnia			
subjects affected / exposed	25 / 228 (10.96%)		
occurrences (all)	25		
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	26 / 228 (11.40%)		
occurrences (all)	35		
Amylase increased			
subjects affected / exposed	27 / 228 (11.84%)		
occurrences (all)	32		
Aspartate aminotransferase increased			
subjects affected / exposed	26 / 228 (11.40%)		
occurrences (all)	37		
Blood alkaline phosphatase increased			
subjects affected / exposed	12 / 228 (5.26%)		
occurrences (all)	13		
Blood creatinine increased			
subjects affected / exposed	18 / 228 (7.89%)		
occurrences (all)	23		
Gamma-glutamyltransferase increased			
subjects affected / exposed	15 / 228 (6.58%)		
occurrences (all)	20		
Lipase increased			

subjects affected / exposed	18 / 228 (7.89%)		
occurrences (all)	21		
Neutrophil count decreased			
subjects affected / exposed	18 / 228 (7.89%)		
occurrences (all)	28		
Platelet count decreased			
subjects affected / exposed	14 / 228 (6.14%)		
occurrences (all)	21		
Weight decreased			
subjects affected / exposed	25 / 228 (10.96%)		
occurrences (all)	26		
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	9 / 228 (3.95%)		
occurrences (all)	10		
Nervous system disorders			
Dizziness			
subjects affected / exposed	34 / 228 (14.91%)		
occurrences (all)	41		
Dysgeusia			
subjects affected / exposed	13 / 228 (5.70%)		
occurrences (all)	15		
Headache			
subjects affected / exposed	30 / 228 (13.16%)		
occurrences (all)	38		
Hypoaesthesia			
subjects affected / exposed	14 / 228 (6.14%)		
occurrences (all)	15		
Neuropathy peripheral			
subjects affected / exposed	25 / 228 (10.96%)		
occurrences (all)	26		
Paraesthesia			
subjects affected / exposed	7 / 228 (3.07%)		
occurrences (all)	7		
Blood and lymphatic system disorders			

Anaemia			
subjects affected / exposed	69 / 228 (30.26%)		
occurrences (all)	101		
Leukopenia			
subjects affected / exposed	10 / 228 (4.39%)		
occurrences (all)	32		
Neutropenia			
subjects affected / exposed	33 / 228 (14.47%)		
occurrences (all)	52		
Thrombocytopenia			
subjects affected / exposed	11 / 228 (4.82%)		
occurrences (all)	17		
Eye disorders			
Lacrimation increased			
subjects affected / exposed	19 / 228 (8.33%)		
occurrences (all)	21		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	14 / 228 (6.14%)		
occurrences (all)	16		
Abdominal pain upper			
subjects affected / exposed	10 / 228 (4.39%)		
occurrences (all)	11		
Constipation			
subjects affected / exposed	57 / 228 (25.00%)		
occurrences (all)	84		
Diarrhoea			
subjects affected / exposed	60 / 228 (26.32%)		
occurrences (all)	90		
Dry mouth			
subjects affected / exposed	6 / 228 (2.63%)		
occurrences (all)	6		
Dyspepsia			
subjects affected / exposed	10 / 228 (4.39%)		
occurrences (all)	18		
Dysphagia			

subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all) Vomiting subjects affected / exposed occurrences (all)	9 / 228 (3.95%) 9 85 / 228 (37.28%) 194 36 / 228 (15.79%) 49		
Skin and subcutaneous tissue disorders Alopecia subjects affected / exposed occurrences (all) Pruritus subjects affected / exposed occurrences (all) Rash subjects affected / exposed occurrences (all) Rash maculo-papular subjects affected / exposed occurrences (all)	 27 / 228 (11.84%) 27 29 / 228 (12.72%) 38 50 / 228 (21.93%) 73 7 / 228 (3.07%) 7		
Renal and urinary disorders Acute kidney injury subjects affected / exposed occurrences (all)	 10 / 228 (4.39%) 10		
Endocrine disorders Hyperthyroidism subjects affected / exposed occurrences (all) Hypothyroidism subjects affected / exposed occurrences (all)	 15 / 228 (6.58%) 17 26 / 228 (11.40%) 27		
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all)	 29 / 228 (12.72%) 39		

Back pain			
subjects affected / exposed	32 / 228 (14.04%)		
occurrences (all)	37		
Bone pain			
subjects affected / exposed	8 / 228 (3.51%)		
occurrences (all)	11		
Muscular weakness			
subjects affected / exposed	11 / 228 (4.82%)		
occurrences (all)	12		
Myalgia			
subjects affected / exposed	10 / 228 (4.39%)		
occurrences (all)	10		
Neck pain			
subjects affected / exposed	8 / 228 (3.51%)		
occurrences (all)	8		
Pain in extremity			
subjects affected / exposed	18 / 228 (7.89%)		
occurrences (all)	20		
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	13 / 228 (5.70%)		
occurrences (all)	20		
Pneumonia			
subjects affected / exposed	10 / 228 (4.39%)		
occurrences (all)	10		
Upper respiratory tract infection			
subjects affected / exposed	18 / 228 (7.89%)		
occurrences (all)	22		
Urinary tract infection			
subjects affected / exposed	18 / 228 (7.89%)		
occurrences (all)	22		
Viral infection			
subjects affected / exposed	7 / 228 (3.07%)		
occurrences (all)	9		
Metabolism and nutrition disorders			

Decreased appetite			
subjects affected / exposed	47 / 228 (20.61%)		
occurrences (all)	57		
Dehydration			
subjects affected / exposed	9 / 228 (3.95%)		
occurrences (all)	13		
Hypercalcaemia			
subjects affected / exposed	7 / 228 (3.07%)		
occurrences (all)	8		
Hyperglycaemia			
subjects affected / exposed	12 / 228 (5.26%)		
occurrences (all)	17		
Hypoalbuminaemia			
subjects affected / exposed	6 / 228 (2.63%)		
occurrences (all)	9		
Hypokalaemia			
subjects affected / exposed	18 / 228 (7.89%)		
occurrences (all)	26		
Hypomagnesaemia			
subjects affected / exposed	16 / 228 (7.02%)		
occurrences (all)	23		
Hyponatraemia			
subjects affected / exposed	11 / 228 (4.82%)		
occurrences (all)	16		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
17 July 2017	Updates to SoA; Serotonin syndrome; clarity to DMC review
17 October 2017	Dose modification and toxicity management guidelines for myocarditis. Melatonin and propofol removed from exclusion criteria and from the list of prohibited medications.
01 May 2018	Amended from a Phase 3 to a Phase 2 design, with ORR as the primary endpoint and PFS, OS, DOR as secondary endpoints due data from the Phase 3 KEYNOTE-252/ECHO-301. Removed Pembro + Epa arm, reduced number of patients to be enrolled to 148 and removed interim analysis.
04 March 2019	Data from the final analysis of KEYNOTE-715/ECHO-306 (data cutoff: 13-DEC-2018) indicated that the study did not meet the prespecified endpoint of improvement in objective response rate (ORR) for the combination of pembrolizumab plus epacadostat plus chemotherapy compared with pembrolizumab plus chemotherapy plus placebo. Based upon these data from the final analysis, the Sponsor and MSD implemented this Amendment 06 to direct that all epacadostat and placebo administration stop and to reflect that the study is no longer blinded. The study remained open so participants still on study will have continued access to pembrolizumab.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

Data from the final analysis of KEYNOTE-715/ECHO-306 (data cutoff: 13-DEC-2018) indicated that the study did not meet the pre-specified endpoint of improvement in objective response rate (ORR).

Notes: