



Clinical trial results:

A Randomized, Double-Blind, Phase III Study of Platinum+Pemetrexed Chemotherapy with or without Pembrolizumab (MK-3475) in First Line Metastatic Non-squamous Non-small Cell Lung Cancer Subjects (KEYNOTE-189)

Summary

EudraCT number	2015-003694-15
Trial protocol	IE DE GB AT BE ES NL FI DK FR
Global end of trial date	22 June 2023

Results information

Result version number	v1 (current)
This version publication date	03 July 2024
First version publication date	03 July 2024

Trial information

Trial identification

Sponsor protocol code	3475-189
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02578680
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Merck Sharp & Dohme LLC
Sponsor organisation address	126 East Lincoln Avenue, P.O. Box 2000, Rahway, NJ, United States, 07065
Public contact	Clinical Trials Disclosure, Merck Sharp & Dohme LLC, ClinicalTrialsDisclosure@merck.com
Scientific contact	Clinical Trials Disclosure, Merck Sharp & Dohme LLC, ClinicalTrialsDisclosure@merck.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	22 June 2023
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	22 June 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This is an efficacy and safety study of pembrolizumab (MK-3475) combined with pemetrexed/platinum chemotherapy versus pemetrexed/platinum chemotherapy alone in participants with advanced or metastatic nonsquamous non-small cell lung cancer (NSCLC) who have not previously received systemic therapy for advanced disease. Participants will be randomly assigned to receive pembrolizumab combined with pemetrexed/platinum (Investigators choice of cisplatin or carboplatin), OR pemetrexed/platinum (Investigators choice of cisplatin or carboplatin). The primary hypothesis is that pembrolizumab in combination with pemetrexed/platinum chemotherapy prolongs Progression-Free Survival (PFS) and Overall Survival (OS) compared to pemetrexed/platinum chemotherapy alone.

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	15 January 2016
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 48
Country: Number of subjects enrolled	Austria: 29
Country: Number of subjects enrolled	Belgium: 10
Country: Number of subjects enrolled	Canada: 38
Country: Number of subjects enrolled	Denmark: 7
Country: Number of subjects enrolled	Finland: 4
Country: Number of subjects enrolled	France: 30
Country: Number of subjects enrolled	Germany: 65
Country: Number of subjects enrolled	Ireland: 11
Country: Number of subjects enrolled	Israel: 27
Country: Number of subjects enrolled	Italy: 58
Country: Number of subjects enrolled	Japan: 10
Country: Number of subjects enrolled	Netherlands: 9
Country: Number of subjects enrolled	Spain: 121
Country: Number of subjects enrolled	United Kingdom: 30
Country: Number of subjects enrolled	United States: 119

Worldwide total number of subjects	616
EEA total number of subjects	344

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)	312
From 65 to 84 years	304
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Eighty-four participants randomized to receive Control switched over to receive pembrolizumab monotherapy. Data from second course treatment contributed to safety data only. All primary and secondary outcome measures are based on protocol-specified cutoff (2017-11-08).

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, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Pembro+Pemetrexed+Platinum ChemoPembro+Pemetrexed

Arm description:

Participants received pembrolizumab 200 mg IV PLUS pemetrexed 500 mg/m² IV (with vitamin supplementation) PLUS cisplatin 75 mg/m² IV OR carboplatin AUC 5 IV on Day 1 of every 3-week cycle (Q3W) for 4 cycles followed by pembrolizumab 200 mg IV PLUS pemetrexed 500 mg/m² IV Q3W until progression. (Participants who received pembrolizumab 200 mg IV Q3W for up to 2 years but experienced disease progression, were eligible to receive a second course of pembrolizumab monotherapy 200 mg IV Q3W, at the investigator's discretion, for up to 1 additional year.)

Arm type	Experimental
Investigational medicinal product name	Pembrolizumab (Pembro)
Investigational medicinal product code	
Other name	KEYTRUDA®, MK-3475, SCH 9000475
Pharmaceutical forms	Concentrate and solvent for concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Pembrolizumab 200 mg IV on Day 1 of every 3-week cycle (Q3W) for 4 cycles followed by pembrolizumab 200 mg IV Q3W until progression.

Investigational medicinal product name	Cisplatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Cisplatin 75 mg/m² IV Day 1 of every 3-week cycle (Q3W) for 4 cycles

Investigational medicinal product name	Vitamin B12 1000 µg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Vitamin B12 1000 µg intramuscular injection in the week preceding the first dose of pemetrexed and once every 3 cycles thereafter. Subsequent vitamin B12 injections may be given the same day as pemetrexed administration.

Investigational medicinal product name	Pemetrexed
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use
Dosage and administration details:	
Pemetrexed 500 mg/m ² IV Q3W	
Investigational medicinal product name	Folic acid 350-1000 µg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
At least 5 doses of folic acid taken during the 7 days preceding the first dose of pemetrexed; folic acid dosing must continue during the full course of therapy and for 21 days after the last dose of pemetrexed	
Investigational medicinal product name	Dexamethasone 4 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
For prophylaxis: dexamethasone 4 mg, orally twice per day (or equivalent). Taken the day before, day of, and day after pemetrexed administration.	
Investigational medicinal product name	Carboplatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use
Dosage and administration details:	
Carboplatin AUC 5 IV on Day 1 of every 3-week cycle (Q3W) for 4 cycles	
Arm title	Control
Arm description:	
Participants received saline placebo IV PLUS pemetrexed 500 mg/m ² IV (with vitamin supplementation) PLUS cisplatin 75 mg/m ² IV OR carboplatin AUC 5 IV on Day 1 of every 3-week cycle (Q3W) for 4 cycles followed by saline placebo IV PLUS pemetrexed 500 mg/m ² IV Q3W until progression. (Effective 23-Dec-2019, participants discontinued saline placebo. If documented disease progression had occurred, and participants receiving Control met certain criteria, they were eligible to switch over to receive pembrolizumab monotherapy Q3W for the remainder of the study.)	
Arm type	Active comparator
Investigational medicinal product name	Saline solution
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use
Dosage and administration details:	
Saline placebo IV PLUS pemetrexed 500 mg/m ² IV (with vitamin supplementation) PLUS cisplatin 75 mg/m ² IV OR carboplatin AUC 5 IV on Day 1 of every 3-week cycle (Q3W) for 4 cycles followed by saline placebo IV PLUS pemetrexed 500 mg/m ² IV Q3W until progression.	
Investigational medicinal product name	Cisplatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:	
Cisplatin 75 mg/m ² IV Day 1 of every 3-week cycle (Q3W) for 4 cycles	
Investigational medicinal product name	Carboplatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use
Dosage and administration details:	
Carboplatin AUC 5 IV on Day 1 of every 3-week cycle (Q3W) for 4 cycles	
Investigational medicinal product name	Dexamethasone 4 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
For prophylaxis: dexamethasone 4 mg, orally twice per day (or equivalent). Taken the day before, day of, and day after pemetrexed administration.	
Investigational medicinal product name	Folic acid 350-1000 µg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
At least 5 doses of folic acid taken during the 7 days preceding the first dose of pemetrexed; folic acid dosing must continue during the full course of therapy and for 21 days after the last dose of pemetrexed	
Investigational medicinal product name	Vitamin B12 1000 µg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use
Dosage and administration details:	
Vitamin B12 1000 µg intramuscular injection in the week preceding the first dose of pemetrexed and once every 3 cycles thereafter. Subsequent vitamin B12 injections may be given the same day as pemetrexed administration.	
Investigational medicinal product name	Pemetrexed
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use
Dosage and administration details:	
Pemetrexed 500 mg/m ² IV Q3W	

Number of subjects in period 1	Pembro+Pemetrexed+Platinum	Control
	ChemoPembro+Pemetrexed	
Started	410	206
Treated	405	202
Switched to Pembrolizumab	0	84

Completed	0	0
Not completed	410	206
Adverse event, serious fatal	329	181
Consent withdrawn by subject	13	9
Physician decision	-	1
Sponsor Decision	64	13
Lost to follow-up	3	1
Protocol deviation	1	1

Baseline characteristics

Reporting groups

Reporting group title	Pembro+Pemetrexed+Platinum ChemoPembro+Pemetrexed
Reporting group description:	
Participants received pembrolizumab 200 mg IV PLUS pemetrexed 500 mg/m ² IV (with vitamin supplementation) PLUS cisplatin 75 mg/m ² IV OR carboplatin AUC 5 IV on Day 1 of every 3-week cycle (Q3W) for 4 cycles followed by pembrolizumab 200 mg IV PLUS pemetrexed 500 mg/m ² IV Q3W until progression. (Participants who received pembrolizumab 200 mg IV Q3W for up to 2 years but experienced disease progression, were eligible to receive a second course of pembrolizumab monotherapy 200 mg IV Q3W, at the investigator's discretion, for up to 1 additional year.)	
Reporting group title	Control
Reporting group description:	
Participants received saline placebo IV PLUS pemetrexed 500 mg/m ² IV (with vitamin supplementation) PLUS cisplatin 75 mg/m ² IV OR carboplatin AUC 5 IV on Day 1 of every 3-week cycle (Q3W) for 4 cycles followed by saline placebo IV PLUS pemetrexed 500 mg/m ² IV Q3W until progression. (Effective 23-Dec-2019, participants discontinued saline placebo. If documented disease progression had occurred, and participants receiving Control met certain criteria, they were eligible to switch over to receive pembrolizumab monotherapy Q3W for the remainder of the study.)	

Reporting group values	Pembro+Pemetrexed+Platinum ChemoPembro+Pemetrexed	Control	Total
Number of subjects	410	206	616
Age categorical			
Units: Subjects			

Age Continuous			
Units: Years			
arithmetic mean	63.2	62.8	
standard deviation	± 9.4	± 9.1	-
Sex: Female, Male			
Units: Participants			
Female	156	97	253
Male	254	109	363
Programmed Cell Death-Ligand 1 (PD-L1) Tumor Status			
Participants were assessed for their PD-L1 tumor expression level by immunohistochemistry assay using tumor tissue from an archival or newly obtained biopsy. Participants with a TPS ≥1% were classified as PD-L1 positive and participants with a TPS <1% were classified as PD-L1 negative.			
Units: Subjects			
TPS <1%	127	63	190
TPS ≥1%	260	128	388
Not Evaluable	23	15	38
Platinum Chemotherapy			
Participants were classified according to the type of platinum chemotherapy the Investigator chose for them to receive: Cisplatin or Carboplatin.			
Units: Subjects			
Cisplatin	113	58	171
Carboplatin	297	148	445
Smoking Status			
Participants were classified according to their smoking status: Never Smoker or Former/Current Smoker.			
Units: Subjects			

Never Smoker	48	25	73
Former/Current Smoker	362	181	543
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	10	8	18
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	11	3	14
White	387	195	582
More than one race	0	0	0
Unknown or Not Reported	2	0	2

End points

End points reporting groups

Reporting group title	Pembro+Pemetrexed+Platinum ChemoPembro+Pemetrexed
Reporting group description: Participants received pembrolizumab 200 mg IV PLUS pemetrexed 500 mg/m ² IV (with vitamin supplementation) PLUS cisplatin 75 mg/m ² IV OR carboplatin AUC 5 IV on Day 1 of every 3-week cycle (Q3W) for 4 cycles followed by pembrolizumab 200 mg IV PLUS pemetrexed 500 mg/m ² IV Q3W until progression. (Participants who received pembrolizumab 200 mg IV Q3W for up to 2 years but experienced disease progression, were eligible to receive a second course of pembrolizumab monotherapy 200 mg IV Q3W, at the investigator's discretion, for up to 1 additional year.)	
Reporting group title	Control
Reporting group description: Participants received saline placebo IV PLUS pemetrexed 500 mg/m ² IV (with vitamin supplementation) PLUS cisplatin 75 mg/m ² IV OR carboplatin AUC 5 IV on Day 1 of every 3-week cycle (Q3W) for 4 cycles followed by saline placebo IV PLUS pemetrexed 500 mg/m ² IV Q3W until progression. (Effective 23-Dec-2019, participants discontinued saline placebo. If documented disease progression had occurred, and participants receiving Control met certain criteria, they were eligible to switch over to receive pembrolizumab monotherapy Q3W for the remainder of the study.)	

Primary: Progression-Free Survival (PFS) Per Response Evaluation Criteria in Solid Tumors (RECIST) 1.1 as Assessed by Blinded Central Imaging (BCI)

End point title	Progression-Free Survival (PFS) Per Response Evaluation Criteria in Solid Tumors (RECIST) 1.1 as Assessed by Blinded Central Imaging (BCI)
End point description: PFS was defined as the time from randomization to the first documented progressive disease (PD) or death due to any cause, whichever occurred first. Per RECIST 1.1, PD was defined as ≥20% increase in the sum of diameters of target lesions, taking as reference the smallest sum on study. In addition to the relative increase of 20%, the sum must also demonstrate an absolute increase of ≥5 mm. Note: The appearance of one or more new lesions was also considered PD. The PFS per RECIST 1.1 is presented. The analysis population for this endpoint consisted of all randomized participants.	
End point type	Primary
End point timeframe: Up to approximately 21 months	

End point values	Pembro+Pemetrexed+Platinum ChemoPembro+Pemetrexed	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	410	206		
Units: Months				
median (confidence interval 95%)	8.8 (7.6 to 9.2)	4.9 (4.7 to 5.5)		

Statistical analyses

Statistical analysis title	PFS Per RECIST 1.1 as Assessed by BCI
Comparison groups	Pembro+Pemetrexed+Platinum ChemoPembro+Pemetrexed v Control
Number of subjects included in analysis	616
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.00001
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.52
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.43
upper limit	0.64

Primary: Overall Survival (OS)

End point title	Overall Survival (OS)
End point description: OS was defined as the time from randomization to death due to any cause. Participants without documented death at the time of the interim analysis were censored at the date of the last follow-up. The OS is presented. The analysis population for this endpoint consisted of all randomized participants. (Note: 99999=Median OS not reached; 99999=Lower Limit OS not reached; and 99999=Upper Limit OS not reached)	
End point type	Primary
End point timeframe: Up to approximately 21 months	

End point values	Pembro+Pemetrexed+Platinum ChemoPembro+Pemetrexed	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	410	206		
Units: Months				
median (confidence interval 95%)	99999 (99999 to 99999)	11.3 (8.7 to 15.1)		

Statistical analyses

Statistical analysis title	Overall Survival
Comparison groups	Pembro+Pemetrexed+Platinum ChemoPembro+Pemetrexed v Control

Number of subjects included in analysis	616
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.00001
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.49
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.38
upper limit	0.64

Secondary: Overall Response Rate (ORR) Per RECIST 1.1 as Assessed by Blinded Central Imaging

End point title	Overall Response Rate (ORR) Per RECIST 1.1 as Assessed by Blinded Central Imaging
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End point description:

ORR was defined as the percentage of participants in the analysis population who had a Complete Response (CR: Disappearance of all target lesions) or a Partial Response (PR: $\geq 30\%$ decrease in the sum of diameters of target lesions, taking as reference the baseline sum diameters) per RECIST 1.1. The percentage of participants who experienced a CR or PR is presented. The analysis population for this endpoint consisted of all randomized participants.

End point type	Secondary
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End point timeframe:

Up to approximately 21 months

End point values	Pembro+Pemetrexed+Platinum ChemoPembro+Pemetrexed	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	410	206		
Units: Percentage of Participants				
number (confidence interval 95%)	47.6 (42.6 to 52.5)	18.9 (13.8 to 25.0)		

Statistical analyses

Statistical analysis title	ORR Per RECIST 1.1 as Assessed by BCI
Comparison groups	Pembro+Pemetrexed+Platinum ChemoPembro+Pemetrexed v Control

Number of subjects included in analysis	616
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001 ^[1]
Method	Stratified Miettinen and Nurminen
Parameter estimate	Difference in Percentage vs. Control
Point estimate	28.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	21.1
upper limit	35.4

Notes:

[1] - H0:Difference in percentages=0 vs H1:Difference in percentages>0

Secondary: Number of Participants Who Discontinued Any Study Drug Due to an AE

End point title	Number of Participants Who Discontinued Any Study Drug Due to an AE
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End point description:

An AE was defined as any untoward medical occurrence in a study participant administered study drug and which does not necessarily have to have a causal relationship with this study drug. The number of participants who discontinued any randomized study drug due to an AE is presented. The analysis population consisted of all randomized participants who received ≥ 1 dose of study drug.

End point type	Secondary
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End point timeframe:

Up to approximately 21 months

End point values	Pembro+Pemetrexed+Platinum	Control		
	ChemoPembro+Pemetrexed			
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	405	202		
Units: Participants	112	30		

Statistical analyses

No statistical analyses for this end point

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

End point title	Number of Participants Who Experienced an Adverse Event (AE)
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End point description:

An AE was defined as any untoward medical occurrence in a study participant administered study drug and which does not necessarily have to have a causal relationship with this study drug. The number of participants who experienced an AE is presented. The analysis population consisted of all randomized participants who received ≥ 1 dose of study drug.

End point type	Secondary
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End point timeframe:

Up to approximately 21 months (Serious AEs: Up to 90 days after last dose of study treatment; Other AEs: Up to 30 days after last dose of study treatment)

End point values	Pembro+Pemetrexed+Platinum ChemoPembro+Pemetrexed	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	405	202		
Units: Participants	404	200		

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (DOR) Per RECIST 1.1 as Assessed by Blinded Central Imaging

End point title	Duration of Response (DOR) Per RECIST 1.1 as Assessed by Blinded Central Imaging
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End point description:

For participants who demonstrated a confirmed CR (disappearance of all target lesions) or PR ($\geq 30\%$ decrease in the sum of diameters of target lesions) per RECIST 1.1, DOR was defined as the time from first documented evidence of a CR or PR until PD or death. DOR for participants who had not progressed or died at the time of analysis was to be censored at the date of their last tumor assessment. Per RECIST 1.1, PD was defined as $\geq 20\%$ increase in the sum of diameters of target lesions. In addition to the relative increase of 20%, the sum must also have demonstrated an absolute increase of ≥ 5 mm. Note: The appearance of one or more new lesions was also considered PD. DOR assessments were based on blinded central imaging review with confirmation. The DOR per RECIST 1.1 for all participants who experienced a confirmed CR or PR is presented. The analysis population consisted of all randomized participants who experienced a confirmed CR or confirmed PR.

End point type	Secondary
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End point timeframe:

Up to approximately 21 months

End point values	Pembro+Pemetrexed+Platinum ChemoPembro+Pemetrexed	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	195	39		
Units: Months				
median (full range (min-max))	11.2 (1.1 to 18.0)	7.8 (2.1 to 16.4)		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Progression-Free Survival (PFS) as Assessed by Investigator Immune-related RECIST (irRECIST) Response Criteria

End point title	Progression-Free Survival (PFS) as Assessed by Investigator Immune-related RECIST (irRECIST) Response Criteria
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End point description:

PFS was defined as the time from randomization to the first documented immune-related progressive disease (irPD) or death due to any cause, whichever occurred first. Per irRECIST, irPD was confirmed if any of the following are observed in 2 scans performed at least 4 weeks apart: target lesion sum of diameters remains ≥ 20 % and at least 5 mm absolute increase compared to nadir; non-target disease resulting in initial PD is qualitatively worse; new lesion resulting in initial irPD is qualitatively worse; additional new lesion(s) since last evaluation; or additional new non-target lesion progression since last evaluation. The PFS per irRECIST 1.1 is presented. The analysis population for this endpoint consisted of all randomized participants.

End point type	Other pre-specified
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End point timeframe:

Up to approximately 39 months

End point values	Pembro+Pemetrexed+Platinum ChemoPembro+Pemetrexed	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	410	206		
Units: Months				
median (confidence interval 95%)	10.3 (9.0 to 11.3)	5.0 (4.8 to 6.0)		

Statistical analyses

Statistical analysis title	PFS as Assessed by Invest irRECIST Rspns Crtra
Comparison groups	Pembro+Pemetrexed+Platinum ChemoPembro+Pemetrexed v Control
Number of subjects included in analysis	616
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.00001
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.49
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.41
upper limit	0.59

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to approximately 88 months

Adverse event reporting additional description:

Safety Pop: Participants receiving ≥ 1 dose of study drug. Deaths (all causes) Pop: All randomized participants. Per protocol, progression of cancer was not considered an AE unless related to study drug. MedDRA preferred terms "Neoplasm progression", "Malignant neoplasm progression", "Disease progression" not related to study drug excluded as AEs.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	26.0
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Reporting groups

Reporting group title	Pembro+Pemetrexed+Platinum ChemoPembro+Pemetrexed
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Reporting group description:

Participants received pembrolizumab 200 mg IV PLUS pemetrexed 500 mg/m² IV (with vitamin supplementation) PLUS cisplatin 75 mg/m² IV OR carboplatin AUC 5 IV on Day 1 of every 3-week cycle (Q3W) for 4 cycles followed by pembrolizumab 200 mg IV PLUS pemetrexed 500 mg/m² IV Q3W until progression. (Participants who received pembrolizumab 200 mg IV Q3W for up to 2 years but experienced disease progression, were eligible to receive a second course of pembrolizumab monotherapy 200 mg IV Q3W, at the investigator's discretion, for up to 1 additional year.)

Reporting group title	Control
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Reporting group description:

Participants received saline placebo IV PLUS pemetrexed 500 mg/m² IV (with vitamin supplementation) PLUS cisplatin 75 mg/m² IV OR carboplatin AUC 5 IV on Day 1 of every 3-week cycle (Q3W) for 4 cycles followed by saline placebo IV PLUS pemetrexed 500 mg/m² IV Q3W until progression. (Effective 23-Dec-2019, participants discontinued saline placebo. If documented disease progression had occurred, and participants receiving Control met certain criteria, they were eligible to switch over to receive pembrolizumab monotherapy Q3W for the remainder of the study.)

Reporting group title	Pembro+Pemetrexed+Platinum ChemoPembro+Pemetrexed, 2nd Course
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Reporting group description:

Participants who received pembrolizumab PLUS pemetrexed and platinum chemotherapy followed by pembrolizumab PLUS pemetrexed during the initial treatment but experienced disease progression, and met certain criteria, received a second course of pembrolizumab monotherapy at 200 mg IV Q3W for up to 1 additional year.

Reporting group title	Control Switched Over to Pembro Monotherapy, 2nd Course
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Reporting group description:

Participants who were switched from saline placebo to receive pembrolizumab monotherapy, and met certain criteria, received a second course of pembrolizumab monotherapy at 200 mg IV Q3W for up to 1 additional year.

Reporting group title	Control Switched Over to Pembro Monotherapy
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Reporting group description:

Qualified participants who received saline placebo with pemetrexed and platinum chemotherapy followed by placebo and pemetrexed, and who experienced disease progression, were switched over to receive pembrolizumab monotherapy 200 mg IV on Day 1 Q3W for up to 2 years.

Serious adverse events	Pembro+Pemetrexed+Platinum ChemoPembro+Pemetrexed	Control	Pembro+Pemetrexed+Platinum ChemoPembro+Pemetrexed, 2nd Course
Total subjects affected by serious			

adverse events			
subjects affected / exposed	233 / 405 (57.53%)	102 / 202 (50.50%)	2 / 9 (22.22%)
number of deaths (all causes)	330	113	4
number of deaths resulting from adverse events	29	14	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Metastases to meninges			
subjects affected / exposed	1 / 405 (0.25%)	0 / 202 (0.00%)	0 / 9 (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
Metastases to central nervous system			
subjects affected / exposed	1 / 405 (0.25%)	0 / 202 (0.00%)	0 / 9 (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	2 / 405 (0.49%)	0 / 202 (0.00%)	0 / 9 (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
Adenocarcinoma of colon			
subjects affected / exposed	0 / 405 (0.00%)	1 / 202 (0.50%)	0 / 9 (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
Bladder cancer			
subjects affected / exposed	0 / 405 (0.00%)	1 / 202 (0.50%)	0 / 9 (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
Cancer pain			
subjects affected / exposed	3 / 405 (0.74%)	2 / 202 (0.99%)	0 / 9 (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
Malignant neoplasm progression			
subjects affected / exposed	0 / 405 (0.00%)	1 / 202 (0.50%)	0 / 9 (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
Tumour pain			

subjects affected / exposed	1 / 405 (0.25%)	0 / 202 (0.00%)	0 / 9 (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
Thyroid cancer			
subjects affected / exposed	1 / 405 (0.25%)	0 / 202 (0.00%)	0 / 9 (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
Squamous cell carcinoma			
subjects affected / exposed	1 / 405 (0.25%)	0 / 202 (0.00%)	0 / 9 (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
Small cell lung cancer			
subjects affected / exposed	1 / 405 (0.25%)	0 / 202 (0.00%)	0 / 9 (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
Tracheal neoplasm			
subjects affected / exposed	0 / 405 (0.00%)	1 / 202 (0.50%)	0 / 9 (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			
Aortic stenosis			
subjects affected / exposed	0 / 405 (0.00%)	1 / 202 (0.50%)	0 / 9 (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
Hypertension			
subjects affected / exposed	2 / 405 (0.49%)	0 / 202 (0.00%)	0 / 9 (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
Deep vein thrombosis			
subjects affected / exposed	2 / 405 (0.49%)	2 / 202 (0.99%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vena cava thrombosis			

subjects affected / exposed	1 / 405 (0.25%)	0 / 202 (0.00%)	0 / 9 (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 artery occlusion			
subjects affected / exposed	1 / 405 (0.25%)	0 / 202 (0.00%)	0 / 9 (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
Jugular vein thrombosis			
subjects affected / exposed	0 / 405 (0.00%)	1 / 202 (0.50%)	0 / 9 (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
Venous occlusion			
subjects affected / exposed	0 / 405 (0.00%)	1 / 202 (0.50%)	0 / 9 (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 disorders and administration site conditions			
Chest pain			
subjects affected / exposed	0 / 405 (0.00%)	1 / 202 (0.50%)	0 / 9 (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	6 / 405 (1.48%)	1 / 202 (0.50%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	3 / 6	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Death			
subjects affected / exposed	3 / 405 (0.74%)	1 / 202 (0.50%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	1 / 3	0 / 1	0 / 0
deaths causally related to treatment / all	1 / 3	0 / 1	0 / 0
General physical health deterioration			
subjects affected / exposed	6 / 405 (1.48%)	2 / 202 (0.99%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	2 / 6	2 / 3	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Fatigue			

subjects affected / exposed	4 / 405 (0.99%)	0 / 202 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	3 / 4	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Inflammation			
subjects affected / exposed	0 / 405 (0.00%)	0 / 202 (0.00%)	0 / 9 (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
Mucosal inflammation			
subjects affected / exposed	0 / 405 (0.00%)	1 / 202 (0.50%)	0 / 9 (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
Malaise			
subjects affected / exposed	0 / 405 (0.00%)	2 / 202 (0.99%)	0 / 9 (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
Localised oedema			
subjects affected / exposed	1 / 405 (0.25%)	0 / 202 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza like illness			
subjects affected / exposed	1 / 405 (0.25%)	0 / 202 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	9 / 405 (2.22%)	5 / 202 (2.48%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	5 / 10	1 / 5	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oedema peripheral			
subjects affected / exposed	2 / 405 (0.49%)	0 / 202 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Multiple organ dysfunction syndrome			

subjects affected / exposed	0 / 405 (0.00%)	1 / 202 (0.50%)	0 / 9 (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
Immune system disorders			
Cytokine release syndrome			
subjects affected / exposed	1 / 405 (0.25%)	0 / 202 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Scrotal cyst			
subjects affected / exposed	1 / 405 (0.25%)	0 / 202 (0.00%)	0 / 9 (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
Balanoposthitis			
subjects affected / exposed	1 / 405 (0.25%)	0 / 202 (0.00%)	0 / 9 (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, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	6 / 405 (1.48%)	3 / 202 (1.49%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	1 / 8	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atelectasis			
subjects affected / exposed	0 / 405 (0.00%)	1 / 202 (0.50%)	0 / 9 (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
Obstructive sleep apnoea syndrome			
subjects affected / exposed	1 / 405 (0.25%)	0 / 202 (0.00%)	0 / 9 (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	13 / 405 (3.21%)	5 / 202 (2.48%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	2 / 14	0 / 6	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonitis			
subjects affected / exposed	13 / 405 (3.21%)	5 / 202 (2.48%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	11 / 13	3 / 5	0 / 0
deaths causally related to treatment / all	2 / 2	0 / 0	0 / 0
Pneumothorax			
subjects affected / exposed	0 / 405 (0.00%)	1 / 202 (0.50%)	0 / 9 (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	6 / 405 (1.48%)	3 / 202 (1.49%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 6	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epistaxis			
subjects affected / exposed	1 / 405 (0.25%)	1 / 202 (0.50%)	0 / 9 (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
Haemoptysis			
subjects affected / exposed	3 / 405 (0.74%)	2 / 202 (0.99%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 0
Haemothorax			
subjects affected / exposed	1 / 405 (0.25%)	0 / 202 (0.00%)	0 / 9 (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
Hiccups			
subjects affected / exposed	1 / 405 (0.25%)	0 / 202 (0.00%)	0 / 9 (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
Obstructive airways disorder			

subjects affected / exposed	1 / 405 (0.25%)	0 / 202 (0.00%)	0 / 9 (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
Pulmonary embolism			
subjects affected / exposed	5 / 405 (1.23%)	4 / 202 (1.98%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 5	1 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary fibrosis			
subjects affected / exposed	1 / 405 (0.25%)	0 / 202 (0.00%)	0 / 9 (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
Pulmonary haemorrhage			
subjects affected / exposed	0 / 405 (0.00%)	0 / 202 (0.00%)	0 / 9 (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 failure			
subjects affected / exposed	1 / 405 (0.25%)	4 / 202 (1.98%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 3	0 / 0
Psychiatric disorders			
Confusional state			
subjects affected / exposed	1 / 405 (0.25%)	0 / 202 (0.00%)	0 / 9 (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
Anxiety			
subjects affected / exposed	1 / 405 (0.25%)	0 / 202 (0.00%)	0 / 9 (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
Major depression			
subjects affected / exposed	1 / 405 (0.25%)	0 / 202 (0.00%)	0 / 9 (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
Disorientation			

subjects affected / exposed	1 / 405 (0.25%)	0 / 202 (0.00%)	0 / 9 (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
Depression			
subjects affected / exposed	1 / 405 (0.25%)	0 / 202 (0.00%)	0 / 9 (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
Delirium			
subjects affected / exposed	0 / 405 (0.00%)	1 / 202 (0.50%)	0 / 9 (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
Product issues			
Device dislocation			
subjects affected / exposed	1 / 405 (0.25%)	0 / 202 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 405 (0.25%)	2 / 202 (0.99%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	1 / 1	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood calcium decreased			
subjects affected / exposed	1 / 405 (0.25%)	0 / 202 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood magnesium decreased			
subjects affected / exposed	1 / 405 (0.25%)	0 / 202 (0.00%)	0 / 9 (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
C-reactive protein increased			
subjects affected / exposed	1 / 405 (0.25%)	0 / 202 (0.00%)	0 / 9 (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
Hepatic enzyme increased			

subjects affected / exposed	1 / 405 (0.25%)	0 / 202 (0.00%)	0 / 9 (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	1 / 405 (0.25%)	0 / 202 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Hip fracture			
subjects affected / exposed	2 / 405 (0.49%)	0 / 202 (0.00%)	0 / 9 (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
Femur fracture			
subjects affected / exposed	1 / 405 (0.25%)	1 / 202 (0.50%)	0 / 9 (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
Femoral neck fracture			
subjects affected / exposed	0 / 405 (0.00%)	1 / 202 (0.50%)	0 / 9 (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	0 / 405 (0.00%)	1 / 202 (0.50%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dislocation of vertebra			
subjects affected / exposed	1 / 405 (0.25%)	0 / 202 (0.00%)	0 / 9 (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
Craniocerebral injury			
subjects affected / exposed	1 / 405 (0.25%)	0 / 202 (0.00%)	0 / 9 (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
Accidental overdose			

subjects affected / exposed	1 / 405 (0.25%)	0 / 202 (0.00%)	0 / 9 (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
Shoulder fracture			
subjects affected / exposed	1 / 405 (0.25%)	0 / 202 (0.00%)	0 / 9 (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
Spinal compression fracture			
subjects affected / exposed	1 / 405 (0.25%)	0 / 202 (0.00%)	0 / 9 (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
Spinal fracture			
subjects affected / exposed	2 / 405 (0.49%)	0 / 202 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Toxicity to various agents			
subjects affected / exposed	1 / 405 (0.25%)	0 / 202 (0.00%)	0 / 9 (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
Upper limb fracture			
subjects affected / exposed	0 / 405 (0.00%)	1 / 202 (0.50%)	0 / 9 (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
Post procedural diarrhoea			
subjects affected / exposed	0 / 405 (0.00%)	1 / 202 (0.50%)	0 / 9 (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
Lumbar vertebral fracture			
subjects affected / exposed	0 / 405 (0.00%)	2 / 202 (0.99%)	0 / 9 (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
Limb traumatic amputation			

subjects affected / exposed	1 / 405 (0.25%)	0 / 202 (0.00%)	0 / 9 (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
Radiation oesophagitis			
subjects affected / exposed	1 / 405 (0.25%)	0 / 202 (0.00%)	0 / 9 (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
Wrist fracture			
subjects affected / exposed	1 / 405 (0.25%)	0 / 202 (0.00%)	0 / 9 (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			
Atrial fibrillation			
subjects affected / exposed	1 / 405 (0.25%)	3 / 202 (1.49%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute myocardial infarction			
subjects affected / exposed	1 / 405 (0.25%)	0 / 202 (0.00%)	0 / 9 (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
Atrial flutter			
subjects affected / exposed	0 / 405 (0.00%)	2 / 202 (0.99%)	0 / 9 (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
Cardiopulmonary failure			
subjects affected / exposed	1 / 405 (0.25%)	0 / 202 (0.00%)	0 / 9 (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 failure			
subjects affected / exposed	4 / 405 (0.99%)	0 / 202 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	1 / 4	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Cardiac arrest			

subjects affected / exposed	2 / 405 (0.49%)	0 / 202 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 2	0 / 0	0 / 0
Left ventricular dysfunction			
subjects affected / exposed	1 / 405 (0.25%)	0 / 202 (0.00%)	0 / 9 (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
Myopericarditis			
subjects affected / exposed	1 / 405 (0.25%)	0 / 202 (0.00%)	0 / 9 (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
Myocardial infarction			
subjects affected / exposed	3 / 405 (0.74%)	0 / 202 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	1 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Pericardial effusion			
subjects affected / exposed	1 / 405 (0.25%)	1 / 202 (0.50%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pericarditis			
subjects affected / exposed	1 / 405 (0.25%)	0 / 202 (0.00%)	0 / 9 (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
Sinus tachycardia			
subjects affected / exposed	3 / 405 (0.74%)	0 / 202 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	1 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stress cardiomyopathy			
subjects affected / exposed	0 / 405 (0.00%)	1 / 202 (0.50%)	0 / 9 (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
Supraventricular tachycardia			

subjects affected / exposed	1 / 405 (0.25%)	1 / 202 (0.50%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Ventricular arrhythmia			
subjects affected / exposed	1 / 405 (0.25%)	0 / 202 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Central nervous system vasculitis			
subjects affected / exposed	1 / 405 (0.25%)	0 / 202 (0.00%)	0 / 9 (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
Brain stem infarction			
subjects affected / exposed	1 / 405 (0.25%)	0 / 202 (0.00%)	0 / 9 (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
Balance disorder			
subjects affected / exposed	1 / 405 (0.25%)	0 / 202 (0.00%)	0 / 9 (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
Cerebral haemorrhage			
subjects affected / exposed	0 / 405 (0.00%)	1 / 202 (0.50%)	0 / 9 (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
Intracranial aneurysm			
subjects affected / exposed	0 / 405 (0.00%)	0 / 202 (0.00%)	0 / 9 (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
Hydrocephalus			
subjects affected / exposed	1 / 405 (0.25%)	0 / 202 (0.00%)	0 / 9 (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
Hemiparesis			

subjects affected / exposed	1 / 405 (0.25%)	0 / 202 (0.00%)	0 / 9 (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
Haemorrhage intracranial			
subjects affected / exposed	0 / 405 (0.00%)	1 / 202 (0.50%)	0 / 9 (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
Encephalopathy			
subjects affected / exposed	1 / 405 (0.25%)	0 / 202 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Dizziness			
subjects affected / exposed	4 / 405 (0.99%)	1 / 202 (0.50%)	0 / 9 (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
Demyelinating polyneuropathy			
subjects affected / exposed	1 / 405 (0.25%)	0 / 202 (0.00%)	0 / 9 (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
Cerebrovascular accident			
subjects affected / exposed	4 / 405 (0.99%)	0 / 202 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral infarction			
subjects affected / exposed	1 / 405 (0.25%)	0 / 202 (0.00%)	0 / 9 (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
Ischaemic stroke			
subjects affected / exposed	2 / 405 (0.49%)	1 / 202 (0.50%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 3	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Seizure			

subjects affected / exposed	2 / 405 (0.49%)	1 / 202 (0.50%)	0 / 9 (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
Partial seizures			
subjects affected / exposed	0 / 405 (0.00%)	1 / 202 (0.50%)	0 / 9 (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
Lumbar radiculopathy			
subjects affected / exposed	1 / 405 (0.25%)	0 / 202 (0.00%)	0 / 9 (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
Lacunar stroke			
subjects affected / exposed	1 / 405 (0.25%)	0 / 202 (0.00%)	0 / 9 (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
Syncope			
subjects affected / exposed	3 / 405 (0.74%)	2 / 202 (0.99%)	0 / 9 (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
Transient ischaemic attack			
subjects affected / exposed	1 / 405 (0.25%)	0 / 202 (0.00%)	0 / 9 (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
Spinal cord compression			
subjects affected / exposed	1 / 405 (0.25%)	0 / 202 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Lymphadenopathy			
subjects affected / exposed	1 / 405 (0.25%)	0 / 202 (0.00%)	0 / 9 (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
Leukopenia			

subjects affected / exposed	3 / 405 (0.74%)	1 / 202 (0.50%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	3 / 3	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anaemia			
subjects affected / exposed	13 / 405 (3.21%)	11 / 202 (5.45%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	10 / 14	11 / 12	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Disseminated intravascular coagulation			
subjects affected / exposed	0 / 405 (0.00%)	1 / 202 (0.50%)	0 / 9 (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
Febrile neutropenia			
subjects affected / exposed	25 / 405 (6.17%)	4 / 202 (1.98%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	24 / 26	4 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopenia			
subjects affected / exposed	13 / 405 (3.21%)	6 / 202 (2.97%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	14 / 14	6 / 6	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancytopenia			
subjects affected / exposed	4 / 405 (0.99%)	2 / 202 (0.99%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	4 / 4	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenia			
subjects affected / exposed	11 / 405 (2.72%)	1 / 202 (0.50%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	8 / 11	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal adhesions			
subjects affected / exposed	1 / 405 (0.25%)	0 / 202 (0.00%)	0 / 9 (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
Abdominal pain upper			

subjects affected / exposed	1 / 405 (0.25%)	2 / 202 (0.99%)	0 / 9 (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
Abdominal pain			
subjects affected / exposed	1 / 405 (0.25%)	0 / 202 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis			
subjects affected / exposed	5 / 405 (1.23%)	0 / 202 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	5 / 5	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal perforation			
subjects affected / exposed	1 / 405 (0.25%)	0 / 202 (0.00%)	0 / 9 (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
Gastritis			
subjects affected / exposed	1 / 405 (0.25%)	0 / 202 (0.00%)	0 / 9 (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
Duodenitis			
subjects affected / exposed	1 / 405 (0.25%)	0 / 202 (0.00%)	0 / 9 (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
Diarrhoea			
subjects affected / exposed	14 / 405 (3.46%)	5 / 202 (2.48%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	13 / 16	5 / 8	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis ulcerative			
subjects affected / exposed	0 / 405 (0.00%)	0 / 202 (0.00%)	0 / 9 (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
Constipation			

subjects affected / exposed	3 / 405 (0.74%)	0 / 202 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lip oedema			
subjects affected / exposed	1 / 405 (0.25%)	0 / 202 (0.00%)	0 / 9 (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
Intussusception			
subjects affected / exposed	1 / 405 (0.25%)	0 / 202 (0.00%)	0 / 9 (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
Intestinal pseudo-obstruction			
subjects affected / exposed	1 / 405 (0.25%)	0 / 202 (0.00%)	0 / 9 (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
Intestinal ischaemia			
subjects affected / exposed	2 / 405 (0.49%)	0 / 202 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 2	0 / 0	0 / 0
Impaired gastric emptying			
subjects affected / exposed	0 / 405 (0.00%)	1 / 202 (0.50%)	0 / 9 (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
Melaena			
subjects affected / exposed	1 / 405 (0.25%)	0 / 202 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal toxicity			
subjects affected / exposed	0 / 405 (0.00%)	0 / 202 (0.00%)	0 / 9 (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
Mesenteric artery embolism			

subjects affected / exposed	1 / 405 (0.25%)	0 / 202 (0.00%)	0 / 9 (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
Pancreatitis acute			
subjects affected / exposed	1 / 405 (0.25%)	0 / 202 (0.00%)	0 / 9 (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
Pancreatitis			
subjects affected / exposed	1 / 405 (0.25%)	0 / 202 (0.00%)	0 / 9 (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
Oesophagitis			
subjects affected / exposed	1 / 405 (0.25%)	1 / 202 (0.50%)	0 / 9 (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
Oesophageal stenosis			
subjects affected / exposed	0 / 405 (0.00%)	1 / 202 (0.50%)	0 / 9 (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
Neutropenic colitis			
subjects affected / exposed	0 / 405 (0.00%)	1 / 202 (0.50%)	0 / 9 (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
Nausea			
subjects affected / exposed	5 / 405 (1.23%)	7 / 202 (3.47%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	4 / 5	3 / 7	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	7 / 405 (1.73%)	5 / 202 (2.48%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	5 / 8	4 / 5	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stomatitis			

subjects affected / exposed	1 / 405 (0.25%)	1 / 202 (0.50%)	0 / 9 (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
Small intestinal haemorrhage			
subjects affected / exposed	1 / 405 (0.25%)	0 / 202 (0.00%)	0 / 9 (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
Pancreatitis chronic			
subjects affected / exposed	1 / 405 (0.25%)	0 / 202 (0.00%)	0 / 9 (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
Hepatobiliary disorders			
Bile duct stone			
subjects affected / exposed	1 / 405 (0.25%)	0 / 202 (0.00%)	0 / 9 (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
Autoimmune hepatitis			
subjects affected / exposed	2 / 405 (0.49%)	0 / 202 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholangitis			
subjects affected / exposed	1 / 405 (0.25%)	0 / 202 (0.00%)	0 / 9 (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
Cholangitis sclerosing			
subjects affected / exposed	1 / 405 (0.25%)	0 / 202 (0.00%)	0 / 9 (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
Immune-mediated hepatitis			
subjects affected / exposed	2 / 405 (0.49%)	0 / 202 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatitis			

subjects affected / exposed	1 / 405 (0.25%)	0 / 202 (0.00%)	0 / 9 (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
Hepatic pain			
subjects affected / exposed	1 / 405 (0.25%)	0 / 202 (0.00%)	0 / 9 (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 / 405 (0.25%)	0 / 202 (0.00%)	0 / 9 (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			
Stasis dermatitis			
subjects affected / exposed	1 / 405 (0.25%)	0 / 202 (0.00%)	0 / 9 (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 sensitisation			
subjects affected / exposed	0 / 405 (0.00%)	1 / 202 (0.50%)	0 / 9 (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
Rash papular			
subjects affected / exposed	1 / 405 (0.25%)	0 / 202 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rash			
subjects affected / exposed	1 / 405 (0.25%)	0 / 202 (0.00%)	0 / 9 (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
Dermatitis			
subjects affected / exposed	0 / 405 (0.00%)	1 / 202 (0.50%)	0 / 9 (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
Renal and urinary disorders			

Acute kidney injury			
subjects affected / exposed	11 / 405 (2.72%)	0 / 202 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	8 / 11	0 / 0	0 / 0
deaths causally related to treatment / all	2 / 2	0 / 0	0 / 0
Nephritis			
subjects affected / exposed	2 / 405 (0.49%)	0 / 202 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematuria			
subjects affected / exposed	0 / 405 (0.00%)	1 / 202 (0.50%)	0 / 9 (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
Chronic kidney disease			
subjects affected / exposed	1 / 405 (0.25%)	0 / 202 (0.00%)	0 / 9 (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
Autoimmune nephritis			
subjects affected / exposed	1 / 405 (0.25%)	0 / 202 (0.00%)	0 / 9 (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
Prerenal failure			
subjects affected / exposed	1 / 405 (0.25%)	0 / 202 (0.00%)	0 / 9 (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
Renal failure			
subjects affected / exposed	1 / 405 (0.25%)	2 / 202 (0.99%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Renal tubular necrosis			
subjects affected / exposed	1 / 405 (0.25%)	1 / 202 (0.50%)	0 / 9 (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
Tubulointerstitial nephritis			

subjects affected / exposed	3 / 405 (0.74%)	0 / 202 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	3 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract obstruction			
subjects affected / exposed	1 / 405 (0.25%)	0 / 202 (0.00%)	0 / 9 (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
Urinary retention			
subjects affected / exposed	1 / 405 (0.25%)	0 / 202 (0.00%)	0 / 9 (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
Endocrine disorders			
Adrenal insufficiency			
subjects affected / exposed	1 / 405 (0.25%)	1 / 202 (0.50%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypothyroidism			
subjects affected / exposed	1 / 405 (0.25%)	0 / 202 (0.00%)	0 / 9 (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			
Arthralgia			
subjects affected / exposed	2 / 405 (0.49%)	0 / 202 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Back pain			
subjects affected / exposed	1 / 405 (0.25%)	1 / 202 (0.50%)	0 / 9 (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
Neck pain			
subjects affected / exposed	1 / 405 (0.25%)	0 / 202 (0.00%)	0 / 9 (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	1 / 405 (0.25%)	0 / 202 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 405 (0.00%)	1 / 202 (0.50%)	0 / 9 (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
Osteolysis			
subjects affected / exposed	1 / 405 (0.25%)	0 / 202 (0.00%)	0 / 9 (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
Hypertrophic osteoarthropathy			
subjects affected / exposed	1 / 405 (0.25%)	0 / 202 (0.00%)	0 / 9 (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
Haematoma muscle			
subjects affected / exposed	1 / 405 (0.25%)	0 / 202 (0.00%)	0 / 9 (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
Groin pain			
subjects affected / exposed	0 / 405 (0.00%)	1 / 202 (0.50%)	0 / 9 (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
Flank pain			
subjects affected / exposed	0 / 405 (0.00%)	1 / 202 (0.50%)	0 / 9 (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
Muscular weakness			
subjects affected / exposed	1 / 405 (0.25%)	0 / 202 (0.00%)	0 / 9 (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
Osteonecrosis of jaw			

subjects affected / exposed	1 / 405 (0.25%)	0 / 202 (0.00%)	0 / 9 (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
Pain in extremity			
subjects affected / exposed	0 / 405 (0.00%)	1 / 202 (0.50%)	0 / 9 (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
Pathological fracture			
subjects affected / exposed	1 / 405 (0.25%)	0 / 202 (0.00%)	0 / 9 (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			
Abdominal sepsis			
subjects affected / exposed	1 / 405 (0.25%)	0 / 202 (0.00%)	0 / 9 (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
Bacteraemia			
subjects affected / exposed	2 / 405 (0.49%)	0 / 202 (0.00%)	0 / 9 (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
Bacillus bacteraemia			
subjects affected / exposed	1 / 405 (0.25%)	0 / 202 (0.00%)	0 / 9 (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
Arthritis bacterial			
subjects affected / exposed	1 / 405 (0.25%)	0 / 202 (0.00%)	0 / 9 (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
Appendicitis			
subjects affected / exposed	1 / 405 (0.25%)	0 / 202 (0.00%)	0 / 9 (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
Bacterial colitis			

subjects affected / exposed	1 / 405 (0.25%)	0 / 202 (0.00%)	0 / 9 (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
Bronchitis			
subjects affected / exposed	4 / 405 (0.99%)	3 / 202 (1.49%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
CNS ventriculitis			
subjects affected / exposed	1 / 405 (0.25%)	0 / 202 (0.00%)	0 / 9 (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
COVID-19 pneumonia			
subjects affected / exposed	1 / 405 (0.25%)	0 / 202 (0.00%)	0 / 9 (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
Diverticulitis			
subjects affected / exposed	1 / 405 (0.25%)	1 / 202 (0.50%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 2	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium difficile colitis			
subjects affected / exposed	1 / 405 (0.25%)	0 / 202 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium difficile infection			
subjects affected / exposed	0 / 405 (0.00%)	1 / 202 (0.50%)	0 / 9 (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 foot infection			
subjects affected / exposed	0 / 405 (0.00%)	1 / 202 (0.50%)	0 / 9 (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
Cellulitis			

subjects affected / exposed	5 / 405 (1.23%)	1 / 202 (0.50%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	5 / 6	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Erysipelas			
subjects affected / exposed	2 / 405 (0.49%)	1 / 202 (0.50%)	0 / 9 (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
Folliculitis			
subjects affected / exposed	1 / 405 (0.25%)	0 / 202 (0.00%)	0 / 9 (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	3 / 405 (0.74%)	0 / 202 (0.00%)	0 / 9 (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
Herpes zoster			
subjects affected / exposed	1 / 405 (0.25%)	0 / 202 (0.00%)	0 / 9 (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
Infected dermal cyst			
subjects affected / exposed	0 / 405 (0.00%)	1 / 202 (0.50%)	0 / 9 (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
Infection			
subjects affected / exposed	2 / 405 (0.49%)	0 / 202 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Empyema			
subjects affected / exposed	1 / 405 (0.25%)	0 / 202 (0.00%)	0 / 9 (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
Encephalitis			

subjects affected / exposed	2 / 405 (0.49%)	0 / 202 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocarditis			
subjects affected / exposed	1 / 405 (0.25%)	0 / 202 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enteritis infectious			
subjects affected / exposed	1 / 405 (0.25%)	0 / 202 (0.00%)	0 / 9 (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
Lower respiratory tract infection			
subjects affected / exposed	4 / 405 (0.99%)	4 / 202 (1.98%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 4	1 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Kidney infection			
subjects affected / exposed	1 / 405 (0.25%)	0 / 202 (0.00%)	0 / 9 (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
Otitis media			
subjects affected / exposed	0 / 405 (0.00%)	1 / 202 (0.50%)	0 / 9 (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 candidiasis			
subjects affected / exposed	1 / 405 (0.25%)	0 / 202 (0.00%)	0 / 9 (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
Neutropenic sepsis			
subjects affected / exposed	2 / 405 (0.49%)	0 / 202 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Lung abscess			

subjects affected / exposed	0 / 405 (0.00%)	1 / 202 (0.50%)	0 / 9 (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
Infectious pleural effusion			
subjects affected / exposed	2 / 405 (0.49%)	0 / 202 (0.00%)	0 / 9 (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
Infective exacerbation of chronic obstructive airways disease			
subjects affected / exposed	0 / 405 (0.00%)	0 / 202 (0.00%)	2 / 9 (22.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza			
subjects affected / exposed	3 / 405 (0.74%)	0 / 202 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	1 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Parotitis			
subjects affected / exposed	0 / 405 (0.00%)	0 / 202 (0.00%)	0 / 9 (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
Pneumonia influenzal			
subjects affected / exposed	1 / 405 (0.25%)	0 / 202 (0.00%)	0 / 9 (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 bacterial			
subjects affected / exposed	1 / 405 (0.25%)	0 / 202 (0.00%)	0 / 9 (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 aspiration			
subjects affected / exposed	2 / 405 (0.49%)	0 / 202 (0.00%)	0 / 9 (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
Pneumonia viral			

subjects affected / exposed	1 / 405 (0.25%)	0 / 202 (0.00%)	0 / 9 (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
Pneumocystis jirovecii pneumonia			
subjects affected / exposed	1 / 405 (0.25%)	0 / 202 (0.00%)	0 / 9 (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
Pneumococcal sepsis			
subjects affected / exposed	1 / 405 (0.25%)	0 / 202 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peritonitis			
subjects affected / exposed	2 / 405 (0.49%)	0 / 202 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	34 / 405 (8.40%)	18 / 202 (8.91%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	6 / 35	2 / 21	0 / 0
deaths causally related to treatment / all	1 / 3	1 / 2	0 / 0
Salmonella bacteraemia			
subjects affected / exposed	0 / 405 (0.00%)	1 / 202 (0.50%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory tract infection			
subjects affected / exposed	2 / 405 (0.49%)	1 / 202 (0.50%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory syncytial virus infection			
subjects affected / exposed	0 / 405 (0.00%)	0 / 202 (0.00%)	0 / 9 (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
Pyelonephritis			

subjects affected / exposed	1 / 405 (0.25%)	0 / 202 (0.00%)	0 / 9 (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
Pulmonary sepsis			
subjects affected / exposed	0 / 405 (0.00%)	1 / 202 (0.50%)	0 / 9 (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
Sepsis			
subjects affected / exposed	7 / 405 (1.73%)	1 / 202 (0.50%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	2 / 7	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	6 / 405 (1.48%)	2 / 202 (0.99%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	1 / 6	0 / 5	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tuberculous pleurisy			
subjects affected / exposed	1 / 405 (0.25%)	0 / 202 (0.00%)	0 / 9 (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
Tuberculosis			
subjects affected / exposed	1 / 405 (0.25%)	0 / 202 (0.00%)	0 / 9 (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
Septic shock			
subjects affected / exposed	1 / 405 (0.25%)	1 / 202 (0.50%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	1 / 1	0 / 0
Upper respiratory tract infection bacterial			
subjects affected / exposed	1 / 405 (0.25%)	0 / 202 (0.00%)	0 / 9 (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
Urinary tract infection			

subjects affected / exposed	5 / 405 (1.23%)	1 / 202 (0.50%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 5	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urosepsis			
subjects affected / exposed	2 / 405 (0.49%)	0 / 202 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 405 (0.00%)	1 / 202 (0.50%)	0 / 9 (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
Dehydration			
subjects affected / exposed	5 / 405 (1.23%)	2 / 202 (0.99%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	3 / 7	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetes mellitus inadequate control			
subjects affected / exposed	1 / 405 (0.25%)	0 / 202 (0.00%)	0 / 9 (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
Hypercalcaemia			
subjects affected / exposed	0 / 405 (0.00%)	0 / 202 (0.00%)	0 / 9 (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
Type 2 diabetes mellitus			
subjects affected / exposed	1 / 405 (0.25%)	0 / 202 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Type 1 diabetes mellitus			
subjects affected / exposed	1 / 405 (0.25%)	0 / 202 (0.00%)	0 / 9 (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
Polydipsia			

subjects affected / exposed	1 / 405 (0.25%)	0 / 202 (0.00%)	0 / 9 (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
Malnutrition			
subjects affected / exposed	1 / 405 (0.25%)	0 / 202 (0.00%)	0 / 9 (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
Hyponatraemia			
subjects affected / exposed	2 / 405 (0.49%)	2 / 202 (0.99%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypomagnesaemia			
subjects affected / exposed	2 / 405 (0.49%)	0 / 202 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypokalaemia			
subjects affected / exposed	1 / 405 (0.25%)	1 / 202 (0.50%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0

Serious adverse events	Control Switched Over to Pembro Monotherapy, 2nd Course	Control Switched Over to Pembro Monotherapy	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 2 (0.00%)	29 / 84 (34.52%)	
number of deaths (all causes)	1	74	
number of deaths resulting from adverse events	0	2	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Metastases to meninges			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastases to central nervous system			

subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostate cancer			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adenocarcinoma of colon			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder cancer			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cancer pain			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malignant neoplasm progression			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tumour pain			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thyroid cancer			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous cell carcinoma			

subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small cell lung cancer			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tracheal neoplasm			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Aortic stenosis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertension			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Deep vein thrombosis			
subjects affected / exposed	0 / 2 (0.00%)	1 / 84 (1.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vena cava thrombosis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral artery occlusion			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Jugular vein thrombosis			

subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Venous occlusion			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	0 / 2 (0.00%)	1 / 84 (1.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Asthenia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Death			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General physical health deterioration			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fatigue			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inflammation			
subjects affected / exposed	0 / 2 (0.00%)	1 / 84 (1.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mucosal inflammation			

subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malaise			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Localised oedema			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza like illness			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	0 / 2 (0.00%)	1 / 84 (1.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oedema peripheral			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple organ dysfunction syndrome			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Cytokine release syndrome			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			

Scrotal cyst			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Balanoposthitis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 2 (0.00%)	1 / 84 (1.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atelectasis			
subjects affected / exposed	0 / 2 (0.00%)	1 / 84 (1.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Obstructive sleep apnoea syndrome			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			
subjects affected / exposed	0 / 2 (0.00%)	1 / 84 (1.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonitis			
subjects affected / exposed	0 / 2 (0.00%)	1 / 84 (1.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumothorax			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Dyspnoea			
subjects affected / exposed	0 / 2 (0.00%)	4 / 84 (4.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 1	
Epistaxis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemoptysis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemothorax			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hiccups			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Obstructive airways disorder			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	0 / 2 (0.00%)	3 / 84 (3.57%)	
occurrences causally related to treatment / all	0 / 0	1 / 4	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pulmonary fibrosis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary haemorrhage			

subjects affected / exposed	0 / 2 (0.00%)	1 / 84 (1.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Confusional state			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anxiety			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Major depression			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Disorientation			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Depression			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Delirium			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Product issues			

Device dislocation subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Alanine aminotransferase increased subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood calcium decreased subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood magnesium decreased subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
C-reactive protein increased subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic enzyme increased subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Platelet count decreased subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Hip fracture subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Femur fracture			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femoral neck fracture			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fall			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dislocation of vertebra			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Craniocerebral injury			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Accidental overdose			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Shoulder fracture			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal compression fracture			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal fracture			

subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Toxicity to various agents			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper limb fracture			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural diarrhoea			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lumbar vertebral fracture			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Limb traumatic amputation			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Radiation oesophagitis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wrist fracture			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Atrial fibrillation			

subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute myocardial infarction			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial flutter			
subjects affected / exposed	0 / 2 (0.00%)	1 / 84 (1.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiopulmonary failure			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac arrest			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Left ventricular dysfunction			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myopericarditis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			

subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericardial effusion			
subjects affected / exposed	0 / 2 (0.00%)	1 / 84 (1.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericarditis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinus tachycardia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stress cardiomyopathy			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Supraventricular tachycardia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular arrhythmia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Central nervous system vasculitis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brain stem infarction			

subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Balance disorder			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral haemorrhage			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intracranial aneurysm			
subjects affected / exposed	0 / 2 (0.00%)	1 / 84 (1.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hydrocephalus			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hemiparesis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhage intracranial			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Encephalopathy			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dizziness			

subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Demyelinating polyneuropathy			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrovascular accident			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral infarction			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic stroke			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seizure			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Partial seizures			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lumbar radiculopathy			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lacunar stroke			

subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient ischaemic attack			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal cord compression			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Lymphadenopathy			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Leukopenia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anaemia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Disseminated intravascular coagulation			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile neutropenia			

subjects affected / exposed	0 / 2 (0.00%)	1 / 84 (1.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancytopenia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal adhesions			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain upper			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain			
subjects affected / exposed	0 / 2 (0.00%)	1 / 84 (1.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal perforation			

subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastritis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenitis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis ulcerative			
subjects affected / exposed	0 / 2 (0.00%)	1 / 84 (1.19%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Constipation			
subjects affected / exposed	0 / 2 (0.00%)	2 / 84 (2.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lip oedema			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intussusception			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal pseudo-obstruction			

subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal ischaemia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Impaired gastric emptying			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Melaena			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal toxicity			
subjects affected / exposed	0 / 2 (0.00%)	1 / 84 (1.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mesenteric artery embolism			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis acute			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophagitis			

subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal stenosis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenic colitis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	0 / 2 (0.00%)	1 / 84 (1.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stomatitis			
subjects affected / exposed	0 / 2 (0.00%)	1 / 84 (1.19%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal haemorrhage			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis chronic			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Bile duct stone			

subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Autoimmune hepatitis			
subjects affected / exposed	0 / 2 (0.00%)	1 / 84 (1.19%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholangitis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholangitis sclerosing			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune-mediated hepatitis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic pain			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Stasis dermatitis			

subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin sensitisation			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rash papular			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rash			
subjects affected / exposed	0 / 2 (0.00%)	1 / 84 (1.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dermatitis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephritis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematuria			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic kidney disease			

subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Autoimmune nephritis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prerenal failure			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal failure			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal tubular necrosis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tubulointerstitial nephritis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract obstruction			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary retention			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Adrenal insufficiency			

subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypothyroidism			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Back pain			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neck pain			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myalgia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal chest pain			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteolysis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertrophic osteoarthropathy			

subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematoma muscle			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Groin pain			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Flank pain			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscular weakness			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteonecrosis of jaw			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain in extremity			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pathological fracture			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Abdominal sepsis			

subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacteraemia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacillus bacteraemia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthritis bacterial			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacterial colitis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	0 / 2 (0.00%)	1 / 84 (1.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
CNS ventriculitis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19 pneumonia			

subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulitis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium difficile colitis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium difficile infection			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic foot infection			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Erysipelas			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Folliculitis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			

subjects affected / exposed	0 / 2 (0.00%)	1 / 84 (1.19%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes zoster			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infected dermal cyst			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infection			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Empyema			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Encephalitis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocarditis			
subjects affected / exposed	0 / 2 (0.00%)	1 / 84 (1.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enteritis infectious			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection			

subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Kidney infection			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Otitis media			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oral candidiasis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenic sepsis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung abscess			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infectious pleural effusion			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infective exacerbation of chronic obstructive airways disease			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			

subjects affected / exposed	0 / 2 (0.00%)	1 / 84 (1.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Parotitis			
subjects affected / exposed	0 / 2 (0.00%)	1 / 84 (1.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia influenzal			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia bacterial			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia aspiration			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia viral			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumocystis jirovecii pneumonia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumococcal sepsis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritonitis			

subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	0 / 2 (0.00%)	4 / 84 (4.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Salmonella bacteraemia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory tract infection			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory syncytial virus infection			
subjects affected / exposed	0 / 2 (0.00%)	1 / 84 (1.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary sepsis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	0 / 2 (0.00%)	1 / 84 (1.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection			

subjects affected / exposed	0 / 2 (0.00%)	1 / 84 (1.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tuberculous pleurisy			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tuberculosis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic shock			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection bacterial			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	0 / 2 (0.00%)	1 / 84 (1.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urosepsis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dehydration			

subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetes mellitus inadequate control			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypercalcaemia			
subjects affected / exposed	0 / 2 (0.00%)	1 / 84 (1.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Type 2 diabetes mellitus			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Type 1 diabetes mellitus			
subjects affected / exposed	0 / 2 (0.00%)	1 / 84 (1.19%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Polydipsia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malnutrition			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyponatraemia			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypomagnesaemia			

subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypokalaemia			
subjects affected / exposed	0 / 2 (0.00%)	1 / 84 (1.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Pembro+Pemetrexed+Platinum ChemoPembro+Pemetrexed	Control	Pembro+Pemetrexed+Platinum ChemoPembro+Pemetrexed, 2nd Course
Total subjects affected by non-serious adverse events			
subjects affected / exposed	395 / 405 (97.53%)	196 / 202 (97.03%)	9 / 9 (100.00%)
Vascular disorders			
Hypertension			
subjects affected / exposed	23 / 405 (5.68%)	11 / 202 (5.45%)	2 / 9 (22.22%)
occurrences (all)	25	14	2
Hypotension			
subjects affected / exposed	24 / 405 (5.93%)	4 / 202 (1.98%)	0 / 9 (0.00%)
occurrences (all)	27	4	0
General disorders and administration site conditions			
Mucosal inflammation			
subjects affected / exposed	37 / 405 (9.14%)	16 / 202 (7.92%)	0 / 9 (0.00%)
occurrences (all)	48	24	0
Fatigue			
subjects affected / exposed	173 / 405 (42.72%)	80 / 202 (39.60%)	1 / 9 (11.11%)
occurrences (all)	285	127	1
Chest pain			
subjects affected / exposed	38 / 405 (9.38%)	12 / 202 (5.94%)	0 / 9 (0.00%)
occurrences (all)	44	14	0
Asthenia			
subjects affected / exposed	85 / 405 (20.99%)	47 / 202 (23.27%)	0 / 9 (0.00%)
occurrences (all)	158	74	0

Oedema peripheral subjects affected / exposed occurrences (all)	103 / 405 (25.43%) 180	35 / 202 (17.33%) 48	0 / 9 (0.00%) 0
Pain subjects affected / exposed occurrences (all)	22 / 405 (5.43%) 22	7 / 202 (3.47%) 7	0 / 9 (0.00%) 0
Pyrexia subjects affected / exposed occurrences (all)	84 / 405 (20.74%) 118	30 / 202 (14.85%) 47	0 / 9 (0.00%) 0
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain subjects affected / exposed occurrences (all)	27 / 405 (6.67%) 33	6 / 202 (2.97%) 6	0 / 9 (0.00%) 0
Dyspnoea subjects affected / exposed occurrences (all)	97 / 405 (23.95%) 118	51 / 202 (25.25%) 59	1 / 9 (11.11%) 1
Epistaxis subjects affected / exposed occurrences (all)	29 / 405 (7.16%) 35	7 / 202 (3.47%) 11	0 / 9 (0.00%) 0
Haemoptysis subjects affected / exposed occurrences (all)	14 / 405 (3.46%) 16	16 / 202 (7.92%) 20	0 / 9 (0.00%) 0
Cough subjects affected / exposed occurrences (all)	104 / 405 (25.68%) 139	62 / 202 (30.69%) 71	2 / 9 (22.22%) 2
Productive cough subjects affected / exposed occurrences (all)	27 / 405 (6.67%) 33	9 / 202 (4.46%) 10	1 / 9 (11.11%) 1
Rhinorrhoea subjects affected / exposed occurrences (all)	25 / 405 (6.17%) 28	10 / 202 (4.95%) 10	1 / 9 (11.11%) 1
Wheezing subjects affected / exposed occurrences (all)	10 / 405 (2.47%) 11	2 / 202 (0.99%) 2	1 / 9 (11.11%) 1
Psychiatric disorders			

Insomnia subjects affected / exposed occurrences (all)	31 / 405 (7.65%) 35	17 / 202 (8.42%) 17	1 / 9 (11.11%) 1
Investigations			
Alanine aminotransferase increased subjects affected / exposed occurrences (all)	50 / 405 (12.35%) 63	19 / 202 (9.41%) 23	0 / 9 (0.00%) 0
Aspartate aminotransferase increased subjects affected / exposed occurrences (all)	40 / 405 (9.88%) 57	13 / 202 (6.44%) 16	0 / 9 (0.00%) 0
Blood alkaline phosphatase increased subjects affected / exposed occurrences (all)	16 / 405 (3.95%) 21	9 / 202 (4.46%) 11	1 / 9 (11.11%) 1
Blood bilirubin increased subjects affected / exposed occurrences (all)	1 / 405 (0.25%) 1	2 / 202 (0.99%) 2	0 / 9 (0.00%) 0
Weight decreased subjects affected / exposed occurrences (all)	44 / 405 (10.86%) 59	16 / 202 (7.92%) 17	0 / 9 (0.00%) 0
Tri-iodothyronine increased subjects affected / exposed occurrences (all)	0 / 405 (0.00%) 0	0 / 202 (0.00%) 0	1 / 9 (11.11%) 1
Blood magnesium decreased subjects affected / exposed occurrences (all)	4 / 405 (0.99%) 4	4 / 202 (1.98%) 4	1 / 9 (11.11%) 1
Blood creatinine increased subjects affected / exposed occurrences (all)	58 / 405 (14.32%) 97	17 / 202 (8.42%) 29	0 / 9 (0.00%) 0
White blood cell count decreased subjects affected / exposed occurrences (all)	28 / 405 (6.91%) 57	13 / 202 (6.44%) 20	0 / 9 (0.00%) 0
Injury, poisoning and procedural complications			
Contusion subjects affected / exposed occurrences (all)	6 / 405 (1.48%) 6	1 / 202 (0.50%) 1	1 / 9 (11.11%) 2
Skin abrasion			

subjects affected / exposed occurrences (all)	1 / 405 (0.25%) 1	2 / 202 (0.99%) 2	1 / 9 (11.11%) 1
Nervous system disorders			
Dysgeusia			
subjects affected / exposed	36 / 405 (8.89%)	17 / 202 (8.42%)	0 / 9 (0.00%)
occurrences (all)	41	17	0
Dizziness			
subjects affected / exposed	58 / 405 (14.32%)	22 / 202 (10.89%)	0 / 9 (0.00%)
occurrences (all)	64	27	0
Headache			
subjects affected / exposed	57 / 405 (14.07%)	22 / 202 (10.89%)	0 / 9 (0.00%)
occurrences (all)	72	29	0
Paraesthesia			
subjects affected / exposed	24 / 405 (5.93%)	14 / 202 (6.93%)	0 / 9 (0.00%)
occurrences (all)	33	21	0
Radiculopathy			
subjects affected / exposed	0 / 405 (0.00%)	0 / 202 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Blood and lymphatic system disorders			
Leukopenia			
subjects affected / exposed	26 / 405 (6.42%)	13 / 202 (6.44%)	0 / 9 (0.00%)
occurrences (all)	44	18	0
Neutropenia			
subjects affected / exposed	108 / 405 (26.67%)	49 / 202 (24.26%)	0 / 9 (0.00%)
occurrences (all)	213	92	0
Anaemia			
subjects affected / exposed	186 / 405 (45.93%)	91 / 202 (45.05%)	0 / 9 (0.00%)
occurrences (all)	253	114	0
Thrombocytopenia			
subjects affected / exposed	68 / 405 (16.79%)	25 / 202 (12.38%)	0 / 9 (0.00%)
occurrences (all)	108	37	0
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	17 / 405 (4.20%)	4 / 202 (1.98%)	1 / 9 (11.11%)
occurrences (all)	21	7	1
Otorrhoea			

subjects affected / exposed occurrences (all)	0 / 405 (0.00%) 0	0 / 202 (0.00%) 0	1 / 9 (11.11%) 1
Ear discomfort subjects affected / exposed occurrences (all)	3 / 405 (0.74%) 3	1 / 202 (0.50%) 1	1 / 9 (11.11%) 1
Tinnitus subjects affected / exposed occurrences (all)	14 / 405 (3.46%) 19	11 / 202 (5.45%) 12	0 / 9 (0.00%) 0
Eye disorders			
Dry eye subjects affected / exposed occurrences (all)	21 / 405 (5.19%) 23	5 / 202 (2.48%) 5	0 / 9 (0.00%) 0
Lacrimation increased subjects affected / exposed occurrences (all)	75 / 405 (18.52%) 87	22 / 202 (10.89%) 24	0 / 9 (0.00%) 0
Gastrointestinal disorders			
Constipation subjects affected / exposed occurrences (all)	143 / 405 (35.31%) 220	67 / 202 (33.17%) 87	0 / 9 (0.00%) 0
Abdominal pain subjects affected / exposed occurrences (all)	39 / 405 (9.63%) 49	13 / 202 (6.44%) 14	2 / 9 (22.22%) 2
Abdominal pain upper subjects affected / exposed occurrences (all)	29 / 405 (7.16%) 31	4 / 202 (1.98%) 4	0 / 9 (0.00%) 0
Dyspepsia subjects affected / exposed occurrences (all)	28 / 405 (6.91%) 31	11 / 202 (5.45%) 11	0 / 9 (0.00%) 0
Diarrhoea subjects affected / exposed occurrences (all)	123 / 405 (30.37%) 179	41 / 202 (20.30%) 54	2 / 9 (22.22%) 2
Gastrooesophageal reflux disease subjects affected / exposed occurrences (all)	17 / 405 (4.20%) 18	6 / 202 (2.97%) 6	1 / 9 (11.11%) 1
Vomiting			

subjects affected / exposed occurrences (all)	104 / 405 (25.68%) 183	43 / 202 (21.29%) 70	1 / 9 (11.11%) 2
Stomatitis subjects affected / exposed occurrences (all)	37 / 405 (9.14%) 54	16 / 202 (7.92%) 21	0 / 9 (0.00%) 0
Nausea subjects affected / exposed occurrences (all)	232 / 405 (57.28%) 430	103 / 202 (50.99%) 186	1 / 9 (11.11%) 2
Skin and subcutaneous tissue disorders			
Skin ulcer subjects affected / exposed occurrences (all)	2 / 405 (0.49%) 2	2 / 202 (0.99%) 2	1 / 9 (11.11%) 1
Alopecia subjects affected / exposed occurrences (all)	22 / 405 (5.43%) 24	10 / 202 (4.95%) 10	0 / 9 (0.00%) 0
Dry skin subjects affected / exposed occurrences (all)	27 / 405 (6.67%) 28	20 / 202 (9.90%) 22	1 / 9 (11.11%) 1
Erythema subjects affected / exposed occurrences (all)	30 / 405 (7.41%) 38	4 / 202 (1.98%) 5	0 / 9 (0.00%) 0
Pruritus subjects affected / exposed occurrences (all)	59 / 405 (14.57%) 80	23 / 202 (11.39%) 25	1 / 9 (11.11%) 1
Rash subjects affected / exposed occurrences (all)	89 / 405 (21.98%) 131	27 / 202 (13.37%) 36	0 / 9 (0.00%) 0
Renal and urinary disorders			
Proteinuria subjects affected / exposed occurrences (all)	4 / 405 (0.99%) 4	0 / 202 (0.00%) 0	2 / 9 (22.22%) 3
Endocrine disorders			
Hypothyroidism subjects affected / exposed occurrences (all)	31 / 405 (7.65%) 38	5 / 202 (2.48%) 7	0 / 9 (0.00%) 0
Musculoskeletal and connective tissue disorders			

Pain in extremity subjects affected / exposed occurrences (all)	37 / 405 (9.14%) 47	18 / 202 (8.91%) 18	1 / 9 (11.11%) 1
Osteoarthritis subjects affected / exposed occurrences (all)	1 / 405 (0.25%) 1	0 / 202 (0.00%) 0	0 / 9 (0.00%) 0
Neck pain subjects affected / exposed occurrences (all)	16 / 405 (3.95%) 16	6 / 202 (2.97%) 8	1 / 9 (11.11%) 1
Musculoskeletal pain subjects affected / exposed occurrences (all)	10 / 405 (2.47%) 13	8 / 202 (3.96%) 9	0 / 9 (0.00%) 0
Musculoskeletal chest pain subjects affected / exposed occurrences (all)	19 / 405 (4.69%) 23	7 / 202 (3.47%) 7	1 / 9 (11.11%) 1
Back pain subjects affected / exposed occurrences (all)	71 / 405 (17.53%) 86	26 / 202 (12.87%) 29	0 / 9 (0.00%) 0
Arthralgia subjects affected / exposed occurrences (all)	70 / 405 (17.28%) 99	28 / 202 (13.86%) 33	1 / 9 (11.11%) 1
Infections and infestations			
Otitis externa subjects affected / exposed occurrences (all)	0 / 405 (0.00%) 0	0 / 202 (0.00%) 0	1 / 9 (11.11%) 1
Nasopharyngitis subjects affected / exposed occurrences (all)	47 / 405 (11.60%) 76	10 / 202 (4.95%) 12	2 / 9 (22.22%) 2
Pneumonia subjects affected / exposed occurrences (all)	21 / 405 (5.19%) 29	6 / 202 (2.97%) 6	0 / 9 (0.00%) 0
Ear infection subjects affected / exposed occurrences (all)	2 / 405 (0.49%) 2	0 / 202 (0.00%) 0	1 / 9 (11.11%) 1
Conjunctivitis			

subjects affected / exposed	37 / 405 (9.14%)	18 / 202 (8.91%)	0 / 9 (0.00%)
occurrences (all)	48	33	0
Bronchitis			
subjects affected / exposed	23 / 405 (5.68%)	6 / 202 (2.97%)	0 / 9 (0.00%)
occurrences (all)	29	7	0
Herpes zoster			
subjects affected / exposed	11 / 405 (2.72%)	2 / 202 (0.99%)	1 / 9 (11.11%)
occurrences (all)	12	2	1
Sinusitis			
subjects affected / exposed	10 / 405 (2.47%)	1 / 202 (0.50%)	1 / 9 (11.11%)
occurrences (all)	12	1	1
Upper respiratory tract infection			
subjects affected / exposed	44 / 405 (10.86%)	16 / 202 (7.92%)	1 / 9 (11.11%)
occurrences (all)	59	17	1
Urinary tract infection			
subjects affected / exposed	34 / 405 (8.40%)	13 / 202 (6.44%)	0 / 9 (0.00%)
occurrences (all)	47	17	0
Metabolism and nutrition disorders			
Hypomagnesaemia			
subjects affected / exposed	37 / 405 (9.14%)	8 / 202 (3.96%)	1 / 9 (11.11%)
occurrences (all)	54	14	1
Hypokalaemia			
subjects affected / exposed	51 / 405 (12.59%)	16 / 202 (7.92%)	0 / 9 (0.00%)
occurrences (all)	91	20	0
Hyperglycaemia			
subjects affected / exposed	34 / 405 (8.40%)	7 / 202 (3.47%)	0 / 9 (0.00%)
occurrences (all)	49	10	0
Decreased appetite			
subjects affected / exposed	122 / 405 (30.12%)	63 / 202 (31.19%)	0 / 9 (0.00%)
occurrences (all)	172	81	0
Hypophosphataemia			
subjects affected / exposed	24 / 405 (5.93%)	5 / 202 (2.48%)	0 / 9 (0.00%)
occurrences (all)	38	13	0

Non-serious adverse events	Control Switched Over to Pembro Monotherapy, 2nd Course	Control Switched Over to Pembro Monotherapy	
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Total subjects affected by non-serious adverse events subjects affected / exposed	2 / 2 (100.00%)	64 / 84 (76.19%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 2 (0.00%)	5 / 84 (5.95%)	
occurrences (all)	0	6	
Hypotension			
subjects affected / exposed	0 / 2 (0.00%)	1 / 84 (1.19%)	
occurrences (all)	0	1	
General disorders and administration site conditions			
Mucosal inflammation			
subjects affected / exposed	0 / 2 (0.00%)	1 / 84 (1.19%)	
occurrences (all)	0	1	
Fatigue			
subjects affected / exposed	0 / 2 (0.00%)	8 / 84 (9.52%)	
occurrences (all)	0	9	
Chest pain			
subjects affected / exposed	0 / 2 (0.00%)	6 / 84 (7.14%)	
occurrences (all)	0	6	
Asthenia			
subjects affected / exposed	0 / 2 (0.00%)	6 / 84 (7.14%)	
occurrences (all)	0	8	
Oedema peripheral			
subjects affected / exposed	0 / 2 (0.00%)	11 / 84 (13.10%)	
occurrences (all)	0	11	
Pain			
subjects affected / exposed	0 / 2 (0.00%)	1 / 84 (1.19%)	
occurrences (all)	0	1	
Pyrexia			
subjects affected / exposed	0 / 2 (0.00%)	6 / 84 (7.14%)	
occurrences (all)	0	7	
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	0 / 2 (0.00%)	1 / 84 (1.19%)	
occurrences (all)	0	1	
Dyspnoea			

subjects affected / exposed	0 / 2 (0.00%)	15 / 84 (17.86%)	
occurrences (all)	0	20	
Epistaxis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences (all)	0	0	
Haemoptysis			
subjects affected / exposed	0 / 2 (0.00%)	2 / 84 (2.38%)	
occurrences (all)	0	2	
Cough			
subjects affected / exposed	0 / 2 (0.00%)	9 / 84 (10.71%)	
occurrences (all)	0	13	
Productive cough			
subjects affected / exposed	0 / 2 (0.00%)	3 / 84 (3.57%)	
occurrences (all)	0	4	
Rhinorrhoea			
subjects affected / exposed	0 / 2 (0.00%)	1 / 84 (1.19%)	
occurrences (all)	0	1	
Wheezing			
subjects affected / exposed	0 / 2 (0.00%)	1 / 84 (1.19%)	
occurrences (all)	0	1	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 2 (0.00%)	1 / 84 (1.19%)	
occurrences (all)	0	1	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 2 (50.00%)	4 / 84 (4.76%)	
occurrences (all)	1	4	
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 2 (50.00%)	5 / 84 (5.95%)	
occurrences (all)	2	6	
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 2 (0.00%)	2 / 84 (2.38%)	
occurrences (all)	0	2	
Blood bilirubin increased			

subjects affected / exposed	1 / 2 (50.00%)	0 / 84 (0.00%)	
occurrences (all)	1	0	
Weight decreased			
subjects affected / exposed	0 / 2 (0.00%)	4 / 84 (4.76%)	
occurrences (all)	0	4	
Tri-iodothyronine increased			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences (all)	0	0	
Blood magnesium decreased			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences (all)	0	0	
Blood creatinine increased			
subjects affected / exposed	1 / 2 (50.00%)	4 / 84 (4.76%)	
occurrences (all)	1	10	
White blood cell count decreased			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences (all)	0	0	
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences (all)	0	0	
Skin abrasion			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences (all)	0	0	
Nervous system disorders			
Dysgeusia			
subjects affected / exposed	0 / 2 (0.00%)	1 / 84 (1.19%)	
occurrences (all)	0	1	
Dizziness			
subjects affected / exposed	0 / 2 (0.00%)	2 / 84 (2.38%)	
occurrences (all)	0	2	
Headache			
subjects affected / exposed	0 / 2 (0.00%)	5 / 84 (5.95%)	
occurrences (all)	0	7	
Paraesthesia			

subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	1 / 84 (1.19%) 1	
Radiculopathy subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	0 / 84 (0.00%) 0	
Blood and lymphatic system disorders Leukopenia subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	0 / 84 (0.00%) 0	
Neutropenia subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	0 / 84 (0.00%) 0	
Anaemia subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	6 / 84 (7.14%) 8	
Thrombocytopenia subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	1 / 84 (1.19%) 1	
Ear and labyrinth disorders Vertigo subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	1 / 84 (1.19%) 2	
Otorrhoea subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	0 / 84 (0.00%) 0	
Ear discomfort subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	0 / 84 (0.00%) 0	
Tinnitus subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	0 / 84 (0.00%) 0	
Eye disorders Dry eye subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	2 / 84 (2.38%) 2	
Lacrimation increased			

subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	1 / 84 (1.19%) 1	
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	0 / 2 (0.00%)	7 / 84 (8.33%)	
occurrences (all)	0	7	
Abdominal pain			
subjects affected / exposed	0 / 2 (0.00%)	7 / 84 (8.33%)	
occurrences (all)	0	7	
Abdominal pain upper			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences (all)	0	0	
Dyspepsia			
subjects affected / exposed	0 / 2 (0.00%)	1 / 84 (1.19%)	
occurrences (all)	0	1	
Diarrhoea			
subjects affected / exposed	0 / 2 (0.00%)	11 / 84 (13.10%)	
occurrences (all)	0	19	
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 2 (0.00%)	2 / 84 (2.38%)	
occurrences (all)	0	2	
Vomiting			
subjects affected / exposed	0 / 2 (0.00%)	12 / 84 (14.29%)	
occurrences (all)	0	14	
Stomatitis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences (all)	0	0	
Nausea			
subjects affected / exposed	0 / 2 (0.00%)	16 / 84 (19.05%)	
occurrences (all)	0	18	
Skin and subcutaneous tissue disorders			
Skin ulcer			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences (all)	0	0	
Alopecia			

subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences (all)	0	0	
Dry skin			
subjects affected / exposed	0 / 2 (0.00%)	1 / 84 (1.19%)	
occurrences (all)	0	1	
Erythema			
subjects affected / exposed	0 / 2 (0.00%)	3 / 84 (3.57%)	
occurrences (all)	0	3	
Pruritus			
subjects affected / exposed	0 / 2 (0.00%)	4 / 84 (4.76%)	
occurrences (all)	0	4	
Rash			
subjects affected / exposed	0 / 2 (0.00%)	4 / 84 (4.76%)	
occurrences (all)	0	4	
Renal and urinary disorders			
Proteinuria			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences (all)	0	0	
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	0 / 2 (0.00%)	6 / 84 (7.14%)	
occurrences (all)	0	6	
Musculoskeletal and connective tissue disorders			
Pain in extremity			
subjects affected / exposed	0 / 2 (0.00%)	6 / 84 (7.14%)	
occurrences (all)	0	7	
Osteoarthritis			
subjects affected / exposed	1 / 2 (50.00%)	0 / 84 (0.00%)	
occurrences (all)	1	0	
Neck pain			
subjects affected / exposed	0 / 2 (0.00%)	4 / 84 (4.76%)	
occurrences (all)	0	4	
Musculoskeletal pain			
subjects affected / exposed	1 / 2 (50.00%)	1 / 84 (1.19%)	
occurrences (all)	1	1	
Musculoskeletal chest pain			

subjects affected / exposed	0 / 2 (0.00%)	2 / 84 (2.38%)	
occurrences (all)	0	2	
Back pain			
subjects affected / exposed	0 / 2 (0.00%)	7 / 84 (8.33%)	
occurrences (all)	0	7	
Arthralgia			
subjects affected / exposed	1 / 2 (50.00%)	10 / 84 (11.90%)	
occurrences (all)	1	12	
Infections and infestations			
Otitis externa			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences (all)	0	0	
Nasopharyngitis			
subjects affected / exposed	0 / 2 (0.00%)	5 / 84 (5.95%)	
occurrences (all)	0	6	
Pneumonia			
subjects affected / exposed	0 / 2 (0.00%)	2 / 84 (2.38%)	
occurrences (all)	0	2	
Ear infection			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences (all)	0	0	
Conjunctivitis			
subjects affected / exposed	0 / 2 (0.00%)	0 / 84 (0.00%)	
occurrences (all)	0	0	
Bronchitis			
subjects affected / exposed	0 / 2 (0.00%)	2 / 84 (2.38%)	
occurrences (all)	0	2	
Herpes zoster			
subjects affected / exposed	0 / 2 (0.00%)	2 / 84 (2.38%)	
occurrences (all)	0	2	
Sinusitis			
subjects affected / exposed	0 / 2 (0.00%)	2 / 84 (2.38%)	
occurrences (all)	0	3	
Upper respiratory tract infection			
subjects affected / exposed	0 / 2 (0.00%)	1 / 84 (1.19%)	
occurrences (all)	0	1	

Urinary tract infection subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	4 / 84 (4.76%) 6	
Metabolism and nutrition disorders			
Hypomagnesaemia subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	0 / 84 (0.00%) 0	
Hypokalaemia subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	2 / 84 (2.38%) 2	
Hyperglycaemia subjects affected / exposed occurrences (all)	1 / 2 (50.00%) 2	2 / 84 (2.38%) 2	
Decreased appetite subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	17 / 84 (20.24%) 19	
Hypophosphataemia subjects affected / exposed occurrences (all)	0 / 2 (0.00%) 0	1 / 84 (1.19%) 1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
03 March 2016	Amendment 02: The primary reason for this protocol amendment was to update the reporting period for all adverse events following cessation of treatment to 30 days.
17 March 2017	Amendment 04: The primary reason for this protocol amendment was to add an OS test at the second interim analysis and the final analysis to achieve at least 88% power; IA1 timing was changed to ~6 months after the last subject had been enrolled; FA would be performed after approximately 369 deaths had been observed.
07 December 2017	Amendment 07: The primary reason for this protocol amendment was to provide a more robust analysis of the data, focusing on OS, and to adjust the alpha spending to most inform the clinical meaningfulness of the data.
29 October 2018	Amendment 09: The primary reason for this protocol amendment was to discontinue pharmacokinetic (PK) and anti-drug antibodies (ADA) sampling and updated pembrolizumab dose justification language based on input from regulatory authorities.
24 February 2020	Amendment 10: The primary reasons for this protocol amendment were to state that final analysis results were positive and that therefore participants were to be given the option of discontinuing placebo treatment.
16 March 2022	Amendment 11: The primary reason for this protocol amendment was to add text to allow participants to rollover to extension study (MK-3475-587).

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported