Clinical trial results:
Randomized, Phase II Study of MK-3475 Versus Chemotherapy in Patients with Advanced Melanoma

Summary

EudraCT number	2012-003030-17
Trial protocol	ES DE NO SE IT NL FR Outside EU/EEA
Global end of trial date	

Results information

Result version number	v1
This version publication date	22 February 2017
First version publication date	22 February 2017

Trial information

Trial identification

Sponsor protocol code	P08719

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01704287
WHO universal trial number (UTN)	-
Other trial identifiers	MK-3475-002: Merck Protocol Number

Notes:

Sponsors

Sponsor organisation name	Merck Sharp & Dohme Corp.
Sponsor organisation address	2000 Galloping Hill Road, Kenilworth, NJ, United States, 07033
Public contact	Clinical Trials Disclosure, Merck Sharp & Dohme Corp., ClinicalTrialsDisclosure@merck.com
Scientific contact	Clinical Trials Disclosure, Merck Sharp & Dohme Corp., ClinicalTrialsDisclosure@merck.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Interim
Date of interim/final analysis	16 November 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	16 November 2015
Global end of trial reached?	No

Notes:

General information about the trial

Main objective of the trial:

This study is being done to compare survival using pembrolizumab (SCH 900475, MK-3475) or standard chemotherapy for participants with advanced melanoma (MEL) who have progressed after prior therapy. Participants were initially randomized to receive either low-dose pembrolizumab, high-dose pembrolizumab or Investigator-choice chemotherapy (ICC) in an open-label fashion. The four standard ICC choices were: carboplatin + paclitaxel, paclitaxel alone, dacarbazine, or temozolomide. Participants on standard chemotherapy who experienced disease progression may have been eligible to switch to treatment with pembrolizumab provided they met protocol-specified requirements for switching. With Amendment 03, all ongoing pembrolizumab and switched participants will be treated with open-label, fixed dose pembrolizumab 200 mg every 3 weeks (Q3W), instead of weight-based dosing of pembrolizumab.

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	20 November 2012
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	Argentina: 2
Country: Number of subjects enrolled	Australia: 10
Country: Number of subjects enrolled	France: 16
Country: Number of subjects enrolled	Germany: 79
Country: Number of subjects enrolled	Israel: 36
Country: Number of subjects enrolled	Italy: 20
Country: Number of subjects enrolled	Netherlands: 36
Country: Number of subjects enrolled	Norway: 5
Country: Number of subjects enrolled	Spain: 16
Country: Number of subjects enrolled	Sweden: 5
Country: Number of subjects enrolled	Switzerland: 36
Country: Number of subjects enrolled	United States: 279
Worldwide total number of subjects	540
EEA total number of subjects	177

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)	1
Adults (18-64 years)	304
From 65 to 84 years	230
85 years and over	5

Subject disposition

Recruitment

Recruitment details:

Participants with advanced melanoma (MEL) refractory to ipilimumab (IPI) were recruited for this study.

Pre-assignment

Screening details:

These results are based on a database cutoff date of 16 Nov 2015, at which time 48 participants were continuing in the study.

Period 1

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

Blinding implementation details:

This was a double-blind treatment period.

Arms

Are arms mutually exclusive?	Yes
Arm title	Pembrolizumab 2 mg/kg

Arm description:

Participants received pembrolizumab 2 mg/kg intravenously (IV) one time every three weeks (Q3W).

Arm type	Experimental
Investigational medicinal product name	Pembrolizumab
Investigational medicinal product code	MK-3475
Other name	KEYTRUDA®
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Pembrolizumab 2 mg/kg IV infusion on Day 1 of each 3-week cycle

Arm title	Pembrolizumab 10 mg/kg

Arm description:

Participants received pembrolizumab 10 mg/kg IV Q3W.

Arm type	Experimental
Investigational medicinal product name	Pembrolizumab
Investigational medicinal product code	MK-3475
Other name	KEYTRUDA®
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Pembrolizumab 10 mg/kg IV infusion on Day 1 of each 3-week cycle

Arm title	Investigator-Choice Chemotherapy (ICC)

Arm description:

Participants received one of four possible chemotherapy regimens decided at the treating institution (carboplatin + paclitaxel, paclitaxel alone, dacarbazine, or temozolomide). Participants who were assigned to ICC, experienced confirmed progression of disease (PD) and met all crossover criteria at study treatment Week 12, had the opportunity to switch to receive pembrolizumab 2 mg/kg or 10 mg/kg in a double-blind fashion.

Arm type	Active comparator

Investigational medicinal product name	Carboplatin
Investigational medicinal product code	
Other name	PARAPLATIN®
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:
Carboplatin per institutional standard.

Investigational medicinal product name	Paclitaxel
Investigational medicinal product code	
Other name	TAXOL®
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:
Paclitaxel per institutional standard.

Investigational medicinal product name	Dacarbazine
Investigational medicinal product code	
Other name	DTIC
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:
Dacarbazine per institutional standard.

Investigational medicinal product name	Temozolomide
Investigational medicinal product code	MK-7365
Other name	TEMODAR®
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:
Temozolomide per institutional standard.

Number of subjects in period 1	Pembrolizumab 2 mg/kg	Pembrolizumab 10 mg/kg	Investigator-Choice Chemotherapy (ICC)
Started	180	181	179
Treated	178	179	171
Completed	0	0	0
Not completed	180	181	179
Consent withdrawn by subject	1	1	4
Death	123	117	128
Unspecified	1	-	-
Continuing in study	52	62	44
Lost to follow-up	3	1	3

Baseline characteristics

Reporting groups	
Reporting group title	Pembrolizumab 2 mg/kg
Reporting group description:	
Participants received pembrolizumab 2 mg/kg intravenously (IV) one time every three weeks (Q3W).	
Reporting group title	Pembrolizumab 10 mg/kg
Reporting group description:	
Participants received pembrolizumab 10 mg/kg IV Q3W.	
Reporting group title	Investigator-Choice Chemotherapy (ICC)
Reporting group description:	
Participants received one of four possible chemotherapy regimens decided at the treating institution (carboplatin + paclitaxel, paclitaxel alone, dacarbazine, or temozolomide). Participants who were assigned to ICC, experienced confirmed progression of disease (PD) and met all crossover criteria at study treatment Week 12, had the opportunity to switch to receive pembrolizumab 2 mg/kg or 10 mg/kg in a double-blind fashion.	

Reporting group values	Pembrolizumab 2 mg/kg	Pembrolizumab 10 mg/kg	Investigator-Choice Chemotherapy (ICC)
Number of subjects	180	181	179
Age Categorical Units: Subjects			
Adolescents (12-17 years)	1	0	0
Adults (18-64 years)	101	106	97
From 65-84 years	77	72	81
85 years and over	1	3	1
Age Continuous Units: years			
arithmetic mean	59.5	60.1	60.5
standard deviation	± 14.9	± 13.3	± 12.7
Gender Categorical Units: Subjects			
Female	76	72	65
Male	104	109	114

Reporting group values	Total		
Number of subjects	540		
Age Categorical Units: Subjects			
Adolescents (12-17 years)	1		
Adults (18-64 years)	304		
From 65-84 years	230		
85 years and over	5		
Age Continuous Units: years arithmetic mean standard deviation	- -		
Gender Categorical Units: Subjects			
Female	213		

Male	327		

Subject analysis sets

Subject analysis set title	Pembrolizumab 2 mg/kg
Subject analysis set type	Safety analysis

Subject analysis set description:

Participants received pembrolizumab 2 mg/kg IV Q3W.

Subject analysis set title	Pembrolizumab 10 mg/kg
Subject analysis set type	Safety analysis

Subject analysis set description:

Participants received pembrolizumab 10 mg/kg IV Q3W.

Subject analysis set title	ICC Only
Subject analysis set type	Safety analysis

Subject analysis set description:

Participants received one of four possible chemotherapy regimens decided at the treating institution (carboplatin + paclitaxel, paclitaxel alone, dacarbazine, or temozolomide). This treatment group included the participants who remained on ICC through the database cutoff date.

Subject analysis set title	ICCPembrolizumab 2 mg/kg
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants who were assigned to ICC, experienced confirmed PD and met all crossover criteria at study treatment Week 12, had the opportunity to switch to receive pembrolizumab 2 mg/kg or 10 mg/kg in a double-blind fashion. Participants who qualified to switch to pembrolizumab, must have completed a washout period of ≥28 days from last dose of chemotherapy before receiving pembrolizumab. Participants received pembrolizumab 2 mg/kg IV Q3W.

Subject analysis set title	ICCPembrolizumab 10 mg/kg
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants who were assigned to ICC, experienced confirmed PD and met all crossover criteria at study treatment Week 12, had the opportunity to switch to receive pembrolizumab 2 mg/kg or 10 mg/kg in a double-blind fashion. Participants who qualified to switch to pembrolizumab, must have completed a washout period of ≥28 days from last dose of chemotherapy before receiving pembrolizumab. Participants received pembrolizumab 10 mg/kg IV Q3W.

Reporting group values	Pembrolizumab 2 mg/kg	Pembrolizumab 10 mg/kg	ICC Only
Number of subjects	178	179	73
Age Categorical Units: Subjects			
Adolescents (12-17 years)	1	0	0
Adults (18-64 years)	99	105	38
From 65-84 years	77	71	34
85 years and over	1	3	1
Age Continuous Units: years			
arithmetic mean	59.7	60.1	61.3
standard deviation	± 14.8	± 13.4	± 12.9
Gender Categorical Units: Subjects			
Female	74	71	23
Male	104	108	50

Reporting group values	ICCPembrolizumab 2 mg/kg	ICCPembrolizumab 10 mg/kg	
Number of subjects	53	45	
Age Categorical Units: Subjects			
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	28	24	
From 65-84 years	25	21	
85 years and over	0	0	
Age Continuous Units: years			
arithmetic mean	59.8	61.3	
standard deviation	± 12.9	± 11.8	
Gender Categorical Units: Subjects			
Female	20	18	
Male	33	27	

End points

End points reporting groups

Reporting group title	Pembrolizumab 2 mg/kg
Reporting group description:	
Participants received pembrolizumab 2 mg/kg intravenously (IV) one time every three weeks (Q3W).	
Reporting group title	Pembrolizumab 10 mg/kg
Reporting group description:	
Participants received pembrolizumab 10 mg/kg IV Q3W.	
Reporting group title	Investigator-Choice Chemotherapy (ICC)
Reporting group description:	
Participants received one of four possible chemotherapy regimens decided at the treating institution (carboplatin + paclitaxel, paclitaxel alone, dacarbazine, or temozolomide). Participants who were assigned to ICC, experienced confirmed progression of disease (PD) and met all crossover criteria at study treatment Week 12, had the opportunity to switch to receive pembrolizumab 2 mg/kg or 10 mg/kg in a double-blind fashion.	
Subject analysis set title	Pembrolizumab 2 mg/kg
Subject analysis set type	Safety analysis
Subject analysis set description:	
Participants received pembrolizumab 2 mg/kg IV Q3W.	
Subject analysis set title	Pembrolizumab 10 mg/kg
Subject analysis set type	Safety analysis
Subject analysis set description:	
Participants received pembrolizumab 10 mg/kg IV Q3W.	
Subject analysis set title	ICC Only
Subject analysis set type	Safety analysis
Subject analysis set description:	
Participants received one of four possible chemotherapy regimens decided at the treating institution (carboplatin + paclitaxel, paclitaxel alone, dacarbazine, or temozolomide). This treatment group included the participants who remained on ICC through the database cutoff date.	
Subject analysis set title	ICCPembrolizumab 2 mg/kg
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants who were assigned to ICC, experienced confirmed PD and met all crossover criteria at study treatment Week 12, had the opportunity to switch to receive pembrolizumab 2 mg/kg or 10 mg/kg in a double-blind fashion. Participants who qualified to switch to pembrolizumab, must have completed a washout period of ≥28 days from last dose of chemotherapy before receiving pembrolizumab. Participants received pembrolizumab 2 mg/kg IV Q3W.	
Subject analysis set title	ICCPembrolizumab 10 mg/kg
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants who were assigned to ICC, experienced confirmed PD and met all crossover criteria at study treatment Week 12, had the opportunity to switch to receive pembrolizumab 2 mg/kg or 10 mg/kg in a double-blind fashion. Participants who qualified to switch to pembrolizumab, must have completed a washout period of ≥28 days from last dose of chemotherapy before receiving pembrolizumab. Participants received pembrolizumab 10 mg/kg IV Q3W.	

Primary: Progression-free Survival (PFS)

End point title	Progression-free Survival (PFS)
End point description:	
PFS was defined as the time from randomization to the first documented disease progression, or death due to any cause, whichever occurred first. Per Response Criteria in Solid Tumors version 1.1 (RECIST 1.1), progressive disease was defined as at least a 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 at least 5 mm. Note: The appearance of one or more new lesions was also considered progression. PFS analysis was based on an integrated radiology	

and oncology (IRO) assessment. PFS was not analyzed for the crossover populations. The Intent-to-Treat (ITT) Population consisted of all randomized participants who had measurable disease at baseline. Participants were included in the treatment group to which they were randomized for the efficacy analysis.

End point type	Primary

End point timeframe:

Up to approximately 33 months

End point values	Pembrolizumab 2 mg/kg	Pembrolizumab 10 mg/kg	Investigator-Choice Chemotherapy (ICC)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	180	181	179	
Units: Months				
median (confidence interval 95%)	2.9 (2.8 to 3.8)	3 (2.8 to 5.2)	2.8 (2.6 to 2.8)	

Statistical analyses

Statistical analysis title	PFS: Pembrolizumab 2 mg/kg v. ICC
Comparison groups	Investigator-Choice Chemotherapy (ICC) v Pembrolizumab 2 mg/kg
Number of subjects included in analysis	359
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [1]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.58
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.46
upper limit	0.73

Notes:

[1] - One-sided p-value based on stratified log-rank test.

Statistical analysis title	PFS: Pembrolizumab 2mg/kg v. Pembrolizumab 10mg/kg
Comparison groups	Pembrolizumab 2 mg/kg v Pembrolizumab 10 mg/kg
Number of subjects included in analysis	361
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1247 [2]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.83

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.66
upper limit	1.05

Notes:

[2] - Two-sided p-value based on stratified log-rank test.

Statistical analysis title	PFS: Pembrolizumab 10 mg/kg v. ICC
Comparison groups	Pembrolizumab 10 mg/kg v Investigator-Choice Chemotherapy (ICC)
Number of subjects included in analysis	360
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [3]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.47
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.37
upper limit	0.6

Notes:

[3] - One-sided p-value based on stratified log-rank test.

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. OS was not analyzed for the crossover populations. The ITT Population consisted of all randomized participants who had measurable disease at baseline. Participants were included in the treatment group to which they were randomized for the efficacy analysis.

End point type	Primary

End point timeframe:

Up to approximately 33 months

End point values	Pembrolizumab 2 mg/kg	Pembrolizumab 10 mg/kg	Investigator-Choice Chemotherapy (ICC)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	180	181	179	
Units: Months				
median (confidence interval 95%)	13.4 (11 to 16.4)	14.7 (11.3 to 19.5)	11 (8.9 to 13.8)	

Statistical analyses

Statistical analysis title	OS: Pembrolizumab 2 mg/kg vs. ICC
Comparison groups	Pembrolizumab 2 mg/kg v Investigator-Choice Chemotherapy (ICC)
Number of subjects included in analysis	359
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1173 [4]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.86
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.67
upper limit	1.1

Notes:

[4] - One-sided p-value based on stratified log-rank test.

Statistical analysis title	OS: Pembrolizumab 2mg/kg vs. Pembrolizumab 10mg/kg
Comparison groups	Pembrolizumab 2 mg/kg v Pembrolizumab 10 mg/kg
Number of subjects included in analysis	361
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2905 [5]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.87
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.67
upper limit	1.12

Notes:

[5] - Two-sided p-value based on stratified log-rank test.

Statistical analysis title	OS: Pembrolizumab 10 mg/kg vs. ICC
Comparison groups	Pembrolizumab 10 mg/kg v Investigator-Choice Chemotherapy (ICC)
Number of subjects included in analysis	360
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0106 [6]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.74

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.57
upper limit	0.96

Notes:

[6] - One-sided p-value based on stratified log-rank test.

Secondary: Best Overall Response

End point title	Best Overall Response

End point description:

The best overall response was assessed by independent radiology review using RECIST 1.1 and was recorded from the start of the study treatment until the end of treatment. Response categories included: Complete Response (CR): disappearance of all target lesions; Partial Response (PR): at least a 30% decrease in the sum of diameters of target lesions; Progressive Disease (PD): at least a 20% increase in the sum of diameters of target lesions; and Stable Disease (SD): neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for PD. Best overall response for the Initial Treatment Period was based on IRO. The analysis population consisted of all randomized participants who had measurable disease at baseline. Participants were included in the initial treatment group to which they were randomized for the efficacy analysis.

End point type	Secondary

End point timeframe:

Up to approximately 33 months

End point values	Pembrolizumab 2 mg/kg	Pembrolizumab 10 mg/kg	Investigator-Choice Chemotherapy (ICC)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	180	181	179	
Units: Percentage of Participants				
number (not applicable)				
Complete Response	3.3	7.2	0	
Partial Response	18.9	20.4	4.5	
Stable Disease	16.7	14.9	19	
Progressive Disease	46.7	47.5	61.5	
Not Evaluable	13.3	9.9	15.1	
No Disease	0.6	0	0	
No Assessment	0.6	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Best Overall Response Among Participants Receiving ICC Who Switched to Receiving Pembrolizumab

End point title	Best Overall Response Among Participants Receiving ICC Who Switched to Receiving Pembrolizumab

End point description:

The best overall response was assessed by independent radiology review using RECIST 1.1 and was recorded from the start of the second line of study treatment until the end of treatment. Response categories included: Complete Response (CR): disappearance of all target lesions; Partial Response (PR): at least a 30% decrease in the sum of diameters of target lesions; Progressive Disease (PD): at least a 20% increase in the sum of diameters of target lesions; and Stable Disease (SD): neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for PD. Best overall response was based based on independent review committee (IRC) for the crossover populations.

End point type	Secondary

End point timeframe:

Up to approximately 29 months

End point values	ICCPembrolizumab 2 mg/kg	ICCPembrolizumab 10 mg/kg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	53	45		
Units: Percentage of Participants				
number (not applicable)				
Complete Response	1.9	4.4		
Partial Response	17	13.3		
Stable Disease	15.1	11.1		
Progressive Disease	54.7	55.6		
Not Evaluable	11.3	13.3		
No Assessment	0	2.2		

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (DOR)

End point title	Duration of Response (DOR)

End point description:

For participants who demonstrated a confirmed response (CR or PR) per RECIST 1.1, response duration was defined as the time from first documented evidence of CR or PR until disease progression or death. Response duration 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. DOR analysis was based on IRO assessment. DOR was not analyzed for the crossover populations. Among participants who demonstrated a confirmed response (CR or PR), the population consisted of all randomized participants who had measurable disease at baseline and who demonstrated a confirmed CR or PR per RECIST 1.1. Participants were included in the treatment group to which they were randomized for the efficacy analysis. 9999=Median DOR not reached. 99999=Upper limit of DOR not reached.

End point type	Secondary

End point timeframe:

Up to approximately 33 months

End point values	Pembrolizumab 2 mg/kg	Pembrolizumab 10 mg/kg	Investigator-Choice Chemotherapy (ICC)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	40	50	8	
Units: Months				
median (full range (min-max))	22.8 (1.4 to 25.3)	9999 (1.1 to 99999)	6.8 (2.8 to 11.3)	

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

An AE is defined as any unfavorable and unintended change in the structure, function, or chemistry of the body temporally associated with the use of the study drug, whether or not considered related to the use of the product. Any worsening (i.e., any clinically significant adverse change in frequency and/or intensity) of a pre-existing condition which is temporally associated with the use of study drug, is also an AE. The Safety Population consisted of all participants who received at least one dose of study drug. AEs are reported based on the study drug taken at the time of the event.

End point type	Secondary

End point timeframe:

Up to approximately 36 months

End point values	Pembrolizumab 2 mg/kg	Pembrolizumab 10 mg/kg	ICC Only	ICCPembrolizumab 2 mg/kg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	178	179	73	53
Units: Participants	172	179	71	53

End point values	ICCPembrolizumab 10 mg/kg			
Subject group type	Subject analysis set			
Number of subjects analysed	45			
Units: Participants	41			

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

An AE is defined as any unfavorable and unintended change in the structure, function, or chemistry of the body temporally associated with the use of the study drug, whether or not considered related to the use of the product. Any worsening (i.e., any clinically significant adverse change in frequency and/or intensity) of a pre-existing condition which is temporally associated with the use of study drug, is also an AE. The Safety Population consisted of all participants who received at least one dose of study drug. AEs are reported based on the study drug taken at the time of the event.

End point type	Secondary

End point timeframe:

Up to approximately 33 months

End point values	Pembrolizumab 2 mg/kg	Pembrolizumab 10 mg/kg	ICC Only	ICCPembrolizumab 2 mg/kg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	178	179	73	53
Units: Participants	27	31	17	4

End point values	ICCPembrolizumab 10 mg/kg			
Subject group type	Subject analysis set			
Number of subjects analysed	45			
Units: Participants	3			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Nonserious AEs: Up to 30 days after last dose of study drug (Up to 34 months); Serious AEs: Up to 90 days after last dose of study drug (Up to 36 months)

Adverse event reporting additional description:

The Safety Population consisted of all participants who received at least one dose of study drug. AEs are reported based on the study drug taken at the time of the event.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18.1

Reporting groups

Reporting group title	ICC (Before Switch to Pembrolizumab 10 mg/kg)

Reporting group description:

Participants received one of four possible chemotherapy regimens (carboplatin + paclitaxel, paclitaxel alone, dacarbazine, or temozolomide). Participants who were assigned to ICC, experienced confirmed PD and met all crossover criteria at study treatment Week 12, had the opportunity to switch to receive pembrolizumab 10 mg/kg. These events occurred while these participants were receiving ICC prior to switching.

Reporting group title	ICC Only

Reporting group description:

Participants received one of four possible chemotherapy regimens decided at the treating institution (carboplatin + paclitaxel, paclitaxel alone, dacarbazine, or temozolomide). This treatment group included the participants who remained on ICC through the database cutoff date.

Reporting group title	ICC (Before Switch to Pembrolizumab 2 mg/kg)

Reporting group description:

Participants received one of four possible chemotherapy regimens (carboplatin + paclitaxel, paclitaxel alone, dacarbazine, or temozolomide). Participants who were assigned to ICC, experienced confirmed PD and met all crossover criteria at study treatment Week 12, had the opportunity to switch to receive pembrolizumab 2 mg/kg. These events occurred while these participants were receiving ICC prior to switching.

Reporting group title	Pembrolizumab 2 mg/kg

Reporting group description:

Participants received pembrolizumab 2 mg/kg IV Q3W.

Reporting group title	Pembrolizumab 10 mg/kg

Reporting group description:

Participants received pembrolizumab 10 mg/kg IV Q3W.

Reporting group title	ICC (After Switch to Pembrolizumab 2 mg/kg)

Reporting group description:

Participants initially received one of four possible chemotherapy regimens (carboplatin + paclitaxel, paclitaxel alone, dacarbazine, or temozolomide), experienced confirmed PD, met all crossover criteria at study treatment Week 12, and switched to receive pembrolizumab 2 mg/kg. These events occurred while these participants were receiving pembrolizumab 2 mg/kg after switching from ICC.

Reporting group title	ICC (After Switch to Pembrolizumab 10 mg/kg)

Reporting group description:

Participants initially received one of four possible chemotherapy regimens (carboplatin + paclitaxel, paclitaxel alone, dacarbazine, or temozolomide), experienced confirmed PD, met all crossover criteria at study treatment Week 12, and switched to receive pembrolizumab 10 mg/kg. These events occurred while these participants were receiving pembrolizumab 10 mg/kg after switching from ICC.

Serious adverse events	ICC (Before Switch to Pembrolizumab 10 mg/kg)	ICC Only	ICC (Before Switch to Pembrolizumab 2 mg/kg)
Total subjects affected by serious adverse events			
subjects affected / exposed	9 / 45 (20.00%)	36 / 73 (49.32%)	15 / 53 (28.30%)
number of deaths (all causes)	0	9	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cancer pain			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (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
Colon cancer metastatic			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (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
Intracranial tumour haemorrhage			
subjects affected / exposed	0 / 45 (0.00%)	1 / 73 (1.37%)	0 / 53 (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
Invasive ductal breast carcinoma			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metastases to central nervous system			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metastases to lymph nodes			

subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metastases to small intestine			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (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
Metastatic pain			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (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
Oncologic complication			
subjects affected / exposed	0 / 45 (0.00%)	1 / 73 (1.37%)	0 / 53 (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
Prostate cancer			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (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
Rectal cancer			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (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
Squamous cell carcinoma of skin			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tumour haemorrhage			
subjects affected / exposed	0 / 45 (0.00%)	1 / 73 (1.37%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tumour pain			

subjects affected / exposed	1 / 45 (2.22%)	0 / 73 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Circulatory collapse			
subjects affected / exposed	0 / 45 (0.00%)	1 / 73 (1.37%)	0 / 53 (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
Deep vein thrombosis			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	1 / 53 (1.89%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhagic infarction			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypotension			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	1 / 53 (1.89%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymphoedema			
subjects affected / exposed	0 / 45 (0.00%)	1 / 73 (1.37%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Orthostatic hypotension			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (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
Phlebitis			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (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
Poor venous access			

subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (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
Venous thrombosis			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (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
Thrombosis			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (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
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (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
Chest pain			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (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
Cyst			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (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
Death			
subjects affected / exposed	0 / 45 (0.00%)	1 / 73 (1.37%)	0 / 53 (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
Device dislocation			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (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
Fatigue			

subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (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
Gait disturbance			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (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
General physical health deterioration			
subjects affected / exposed	0 / 45 (0.00%)	2 / 73 (2.74%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Generalised oedema			
subjects affected / exposed	0 / 45 (0.00%)	1 / 73 (1.37%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Infusion site extravasation			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (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
Malaise			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oedema			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (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
Pyrexia			
subjects affected / exposed	1 / 45 (2.22%)	1 / 73 (1.37%)	0 / 53 (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
Immune system disorders			
Anaphylactic reaction			

subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (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
Hypersensitivity			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (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
Cytokine release syndrome			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (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
Reproductive system and breast disorders			
Pelvic pain			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	1 / 53 (1.89%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cough			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (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
Dyspnoea			
subjects affected / exposed	1 / 45 (2.22%)	3 / 73 (4.11%)	0 / 53 (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
Dyspnoea exertional			

subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (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
Epistaxis			
subjects affected / exposed	0 / 45 (0.00%)	1 / 73 (1.37%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemoptysis			
subjects affected / exposed	0 / 45 (0.00%)	1 / 73 (1.37%)	0 / 53 (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
Haemothorax			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (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
Hypoxia			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (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
Interstitial lung disease			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (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
Laryngeal inflammation			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (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 aspiration			

subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (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
Pneumonitis			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (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
Pneumothorax			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (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
Pulmonary embolism			
subjects affected / exposed	0 / 45 (0.00%)	2 / 73 (2.74%)	2 / 53 (3.77%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Pulmonary thrombosis			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (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
Acute respiratory failure			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (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
Alveolitis allergic			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (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
Psychiatric disorders			
Confusional state			
subjects affected / exposed	0 / 45 (0.00%)	1 / 73 (1.37%)	0 / 53 (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
Delirium			

subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (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
Mental status changes			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (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
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (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
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (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
Hepatic enzyme increased			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (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
Neutrophil count decreased			
subjects affected / exposed	0 / 45 (0.00%)	1 / 73 (1.37%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Platelet count decreased			
subjects affected / exposed	0 / 45 (0.00%)	2 / 73 (2.74%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
White blood cell count decreased			
subjects affected / exposed	0 / 45 (0.00%)	1 / 73 (1.37%)	0 / 53 (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
Injury, poisoning and procedural complications			

Fall			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (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
Femur fracture			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	1 / 53 (1.89%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fracture displacement			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (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
Hip fracture			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (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
Lower limb fracture			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (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
Rib fracture			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (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
Spinal fracture			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (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
Subdural haematoma			
subjects affected / exposed	0 / 45 (0.00%)	1 / 73 (1.37%)	0 / 53 (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
Traumatic intracranial haemorrhage			

subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (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
Wound			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (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
Accidental overdose			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (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
Atrioventricular block complete			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac ventricular disorder			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (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
Cardiogenic shock			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (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
Myocardial infarction			

subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	1 / 53 (1.89%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pericardial effusion			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Ataxia			
subjects affected / exposed	0 / 45 (0.00%)	1 / 73 (1.37%)	0 / 53 (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
Cerebrovascular accident			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (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
Dizziness			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (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
Encephalopathy			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (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
Epilepsy			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhage intracranial			
subjects affected / exposed	0 / 45 (0.00%)	1 / 73 (1.37%)	0 / 53 (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
Hemiparesis			

subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (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
Hemiplegia			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (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
Lumbar radiculopathy			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (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
Meningitis noninfective			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (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
Myasthenic syndrome			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (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
Myoclonus			
subjects affected / exposed	0 / 45 (0.00%)	1 / 73 (1.37%)	0 / 53 (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
Neuropathy peripheral			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (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
Paraesthesia			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (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
Partial seizures			

subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (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
Presyncope			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (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
Sciatica			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seizure			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (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
Spinal cord compression			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (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
Syncope			
subjects affected / exposed	0 / 45 (0.00%)	1 / 73 (1.37%)	0 / 53 (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
Transient ischaemic attack			
subjects affected / exposed	0 / 45 (0.00%)	1 / 73 (1.37%)	0 / 53 (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
Depressed level of consciousness			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (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
Peripheral motor neuropathy			

subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 45 (0.00%)	3 / 73 (4.11%)	1 / 53 (1.89%)
occurrences causally related to treatment / all	0 / 0	2 / 3	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bone marrow failure			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (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
Febrile neutropenia			
subjects affected / exposed	0 / 45 (0.00%)	2 / 73 (2.74%)	1 / 53 (1.89%)
occurrences causally related to treatment / all	0 / 0	2 / 2	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Leukopenia			
subjects affected / exposed	0 / 45 (0.00%)	1 / 73 (1.37%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenia			
subjects affected / exposed	0 / 45 (0.00%)	1 / 73 (1.37%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopenia			
subjects affected / exposed	0 / 45 (0.00%)	2 / 73 (2.74%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
Vertigo positional			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			

Eye movement disorder			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (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
Iritis			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 45 (0.00%)	1 / 73 (1.37%)	0 / 53 (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
Ascites			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	1 / 53 (1.89%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Autoimmune colitis			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis			
subjects affected / exposed	0 / 45 (0.00%)	1 / 73 (1.37%)	0 / 53 (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
Constipation			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	1 / 53 (1.89%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	1 / 45 (2.22%)	0 / 73 (0.00%)	0 / 53 (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
Diverticulum			

subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (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
Dysphagia			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric disorder			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorder			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal pain			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (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
Haematemesis			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (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
Haematochezia			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	1 / 53 (1.89%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ileus			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (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
Intestinal obstruction			

subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (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
Intussusception			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (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
Large intestinal ulcer			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (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
Large intestine perforation			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (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
Malabsorption			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	0 / 45 (0.00%)	3 / 73 (4.11%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	3 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Odynophagia			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (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
Pancreatitis			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (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
Rectal haemorrhage			

subjects affected / exposed	0 / 45 (0.00%)	1 / 73 (1.37%)	0 / 53 (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
Small intestinal obstruction			
subjects affected / exposed	0 / 45 (0.00%)	1 / 73 (1.37%)	0 / 53 (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
Small intestinal perforation			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (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
Upper gastrointestinal haemorrhage			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 45 (0.00%)	1 / 73 (1.37%)	0 / 53 (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
Lower gastrointestinal haemorrhage			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (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
Hepatobiliary disorders			
Autoimmune hepatitis			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (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
Cholangitis			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (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
Cholecystitis			

subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (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
Hepatic failure			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (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
Hepatic necrosis			
subjects affected / exposed	0 / 45 (0.00%)	1 / 73 (1.37%)	0 / 53 (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
Hyperbilirubinaemia			
subjects affected / exposed	1 / 45 (2.22%)	0 / 73 (0.00%)	0 / 53 (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
Bile duct obstruction			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Lichenoid keratosis			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (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
Rash maculo-papular			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin mass			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (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
Stevens-Johnson syndrome			

subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (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
Purpura			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	1 / 53 (1.89%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hydronephrosis			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (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
Obstructive uropathy			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (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
Postrenal failure			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal failure			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (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
Tubulointerstitial nephritis			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal impairment			

subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (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
Endocrine disorders			
Addison's disease			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	1 / 53 (1.89%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Adrenal insufficiency			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (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
Adrenocortical insufficiency acute			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (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
Hyperparathyroidism			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypophysitis			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (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
Hypopituitarism			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (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
Secondary adrenocortical insufficiency			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (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
Inappropriate antidiuretic hormone secretion			

subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (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
Back pain			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (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
Groin pain			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Muscular weakness			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal pain			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (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
Neck pain			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (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
Osteolysis			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (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
Pain in extremity			

subjects affected / exposed	1 / 45 (2.22%)	0 / 73 (0.00%)	0 / 53 (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
Spondylolisthesis			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (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
Cervical spinal stenosis			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Appendicitis perforated			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (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
Atypical pneumonia			
subjects affected / exposed	0 / 45 (0.00%)	1 / 73 (1.37%)	0 / 53 (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
Bacteraemia			
subjects affected / exposed	0 / 45 (0.00%)	1 / 73 (1.37%)	0 / 53 (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
Bronchitis			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (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
Candida infection			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (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
Cellulitis			

subjects affected / exposed	0 / 45 (0.00%)	1 / 73 (1.37%)	0 / 53 (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 streptococcal			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (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
Clostridium difficile colitis			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (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
Diverticulitis			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (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
Enterocolitis infectious			
subjects affected / exposed	0 / 45 (0.00%)	1 / 73 (1.37%)	0 / 53 (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
Erysipelas			
subjects affected / exposed	0 / 45 (0.00%)	1 / 73 (1.37%)	1 / 53 (1.89%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis viral			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (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
Herpes zoster			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (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
Infected cyst			

subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (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
Infection			
subjects affected / exposed	0 / 45 (0.00%)	2 / 73 (2.74%)	0 / 53 (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
Infectious pleural effusion			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (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
Influenza			
subjects affected / exposed	1 / 45 (2.22%)	0 / 73 (0.00%)	0 / 53 (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
Mastitis			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (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
Osteomyelitis			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (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
Pelvic abscess			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (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			
subjects affected / exposed	2 / 45 (4.44%)	3 / 73 (4.11%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Respiratory syncytial virus infection			

subjects affected / exposed	1 / 45 (2.22%)	0 / 73 (0.00%)	0 / 53 (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
Salmonellosis			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (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
Sepsis			
subjects affected / exposed	0 / 45 (0.00%)	2 / 73 (2.74%)	1 / 53 (1.89%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic shock			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin infection			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (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
Soft tissue infection			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	1 / 53 (1.89%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Streptococcal sepsis			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 45 (0.00%)	2 / 73 (2.74%)	0 / 53 (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
Viral infection			

subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (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
Viral upper respiratory tract infection			
subjects affected / exposed	1 / 45 (2.22%)	0 / 73 (0.00%)	0 / 53 (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
Wound infection			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (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
Lung infection			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (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
Postoperative wound infection			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (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
Urosepsis			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (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
Metabolism and nutrition disorders			
Cachexia			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dehydration			
subjects affected / exposed	0 / 45 (0.00%)	1 / 73 (1.37%)	1 / 53 (1.89%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetic metabolic decompensation			

subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypercalcaemia			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperglycaemia			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (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
Hypocalcaemia			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	1 / 53 (1.89%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemia			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (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

Serious adverse events	Pembrolizumab 2 mg/kg	Pembrolizumab 10 mg/kg	ICC (After Switch to Pembrolizumab 2 mg/kg)
Total subjects affected by serious adverse events			
subjects affected / exposed	94 / 178 (52.81%)	78 / 179 (43.58%)	17 / 53 (32.08%)
number of deaths (all causes)	15	10	1
number of deaths resulting from adverse events	1	1	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	2 / 178 (1.12%)	0 / 179 (0.00%)	0 / 53 (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
Cancer pain			

subjects affected / exposed	0 / 178 (0.00%)	1 / 179 (0.56%)	0 / 53 (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
Colon cancer metastatic			
subjects affected / exposed	0 / 178 (0.00%)	1 / 179 (0.56%)	0 / 53 (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
Intracranial tumour haemorrhage			
subjects affected / exposed	0 / 178 (0.00%)	0 / 179 (0.00%)	1 / 53 (1.89%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Invasive ductal breast carcinoma			
subjects affected / exposed	1 / 178 (0.56%)	0 / 179 (0.00%)	0 / 53 (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	3 / 178 (1.69%)	1 / 179 (0.56%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metastases to lymph nodes			
subjects affected / exposed	1 / 178 (0.56%)	0 / 179 (0.00%)	0 / 53 (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 small intestine			
subjects affected / exposed	1 / 178 (0.56%)	0 / 179 (0.00%)	0 / 53 (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
Metastatic pain			
subjects affected / exposed	1 / 178 (0.56%)	0 / 179 (0.00%)	0 / 53 (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
Oncologic complication			

subjects affected / exposed	1 / 178 (0.56%)	0 / 179 (0.00%)	0 / 53 (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	1 / 178 (0.56%)	0 / 179 (0.00%)	0 / 53 (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
Rectal cancer			
subjects affected / exposed	0 / 178 (0.00%)	1 / 179 (0.56%)	0 / 53 (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
Squamous cell carcinoma of skin			
subjects affected / exposed	1 / 178 (0.56%)	1 / 179 (0.56%)	0 / 53 (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
Tumour haemorrhage			
subjects affected / exposed	0 / 178 (0.00%)	0 / 179 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tumour pain			
subjects affected / exposed	2 / 178 (1.12%)	0 / 179 (0.00%)	1 / 53 (1.89%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Circulatory collapse			
subjects affected / exposed	0 / 178 (0.00%)	0 / 179 (0.00%)	0 / 53 (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
Deep vein thrombosis			
subjects affected / exposed	1 / 178 (0.56%)	1 / 179 (0.56%)	0 / 53 (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
Haemorrhagic infarction			

subjects affected / exposed	1 / 178 (0.56%)	0 / 179 (0.00%)	0 / 53 (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
Hypotension			
subjects affected / exposed	1 / 178 (0.56%)	0 / 179 (0.00%)	1 / 53 (1.89%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymphoedema			
subjects affected / exposed	0 / 178 (0.00%)	0 / 179 (0.00%)	0 / 53 (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
Orthostatic hypotension			
subjects affected / exposed	0 / 178 (0.00%)	1 / 179 (0.56%)	0 / 53 (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
Phlebitis			
subjects affected / exposed	1 / 178 (0.56%)	0 / 179 (0.00%)	0 / 53 (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
Poor venous access			
subjects affected / exposed	1 / 178 (0.56%)	0 / 179 (0.00%)	0 / 53 (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
Venous thrombosis			
subjects affected / exposed	0 / 178 (0.00%)	1 / 179 (0.56%)	0 / 53 (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
Thrombosis			
subjects affected / exposed	0 / 178 (0.00%)	0 / 179 (0.00%)	0 / 53 (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
General disorders and administration site conditions			
Asthenia			

subjects affected / exposed	1 / 178 (0.56%)	1 / 179 (0.56%)	0 / 53 (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
Chest pain			
subjects affected / exposed	2 / 178 (1.12%)	0 / 179 (0.00%)	0 / 53 (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
Cyst			
subjects affected / exposed	0 / 178 (0.00%)	1 / 179 (0.56%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Death			
subjects affected / exposed	2 / 178 (1.12%)	2 / 179 (1.12%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 2	0 / 2	0 / 0
Device dislocation			
subjects affected / exposed	1 / 178 (0.56%)	0 / 179 (0.00%)	0 / 53 (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
Fatigue			
subjects affected / exposed	0 / 178 (0.00%)	1 / 179 (0.56%)	0 / 53 (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
Gait disturbance			
subjects affected / exposed	1 / 178 (0.56%)	0 / 179 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General physical health deterioration			
subjects affected / exposed	2 / 178 (1.12%)	6 / 179 (3.35%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 2	1 / 6	0 / 0
deaths causally related to treatment / all	0 / 2	1 / 3	0 / 0
Generalised oedema			

subjects affected / exposed	3 / 178 (1.69%)	0 / 179 (0.00%)	1 / 53 (1.89%)
occurrences causally related to treatment / all	2 / 3	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Infusion site extravasation			
subjects affected / exposed	0 / 178 (0.00%)	1 / 179 (0.56%)	0 / 53 (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
Malaise			
subjects affected / exposed	1 / 178 (0.56%)	0 / 179 (0.00%)	0 / 53 (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
Oedema			
subjects affected / exposed	1 / 178 (0.56%)	0 / 179 (0.00%)	0 / 53 (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	3 / 178 (1.69%)	4 / 179 (2.23%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 5	1 / 5	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	0 / 178 (0.00%)	1 / 179 (0.56%)	0 / 53 (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
Hypersensitivity			
subjects affected / exposed	0 / 178 (0.00%)	1 / 179 (0.56%)	0 / 53 (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
Cytokine release syndrome			
subjects affected / exposed	0 / 178 (0.00%)	0 / 179 (0.00%)	0 / 53 (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
Reproductive system and breast disorders			

Pelvic pain			
subjects affected / exposed	1 / 178 (0.56%)	0 / 179 (0.00%)	0 / 53 (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	2 / 178 (1.12%)	0 / 179 (0.00%)	1 / 53 (1.89%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cough			
subjects affected / exposed	1 / 178 (0.56%)	0 / 179 (0.00%)	0 / 53 (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
Dyspnoea			
subjects affected / exposed	3 / 178 (1.69%)	5 / 179 (2.79%)	1 / 53 (1.89%)
occurrences causally related to treatment / all	1 / 3	0 / 5	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 2	0 / 0
Dyspnoea exertional			
subjects affected / exposed	1 / 178 (0.56%)	0 / 179 (0.00%)	0 / 53 (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
Epistaxis			
subjects affected / exposed	1 / 178 (0.56%)	0 / 179 (0.00%)	0 / 53 (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
Haemoptysis			
subjects affected / exposed	1 / 178 (0.56%)	0 / 179 (0.00%)	0 / 53 (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
Haemothorax			
subjects affected / exposed	1 / 178 (0.56%)	0 / 179 (0.00%)	0 / 53 (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

Hypoxia			
subjects affected / exposed	0 / 178 (0.00%)	1 / 179 (0.56%)	0 / 53 (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
Interstitial lung disease			
subjects affected / exposed	1 / 178 (0.56%)	1 / 179 (0.56%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Laryngeal inflammation			
subjects affected / exposed	1 / 178 (0.56%)	0 / 179 (0.00%)	0 / 53 (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
Pleural effusion			
subjects affected / exposed	1 / 178 (0.56%)	1 / 179 (0.56%)	0 / 53 (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
Pneumonia aspiration			
subjects affected / exposed	0 / 178 (0.00%)	1 / 179 (0.56%)	0 / 53 (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
Pneumonitis			
subjects affected / exposed	1 / 178 (0.56%)	3 / 179 (1.68%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	1 / 1	3 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumothorax			
subjects affected / exposed	0 / 178 (0.00%)	1 / 179 (0.56%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	2 / 178 (1.12%)	1 / 179 (0.56%)	1 / 53 (1.89%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary thrombosis			

subjects affected / exposed	0 / 178 (0.00%)	1 / 179 (0.56%)	0 / 53 (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
Acute respiratory failure			
subjects affected / exposed	0 / 178 (0.00%)	0 / 179 (0.00%)	1 / 53 (1.89%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Alveolitis allergic			
subjects affected / exposed	0 / 178 (0.00%)	0 / 179 (0.00%)	1 / 53 (1.89%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Confusional state			
subjects affected / exposed	2 / 178 (1.12%)	3 / 179 (1.68%)	1 / 53 (1.89%)
occurrences causally related to treatment / all	0 / 2	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Delirium			
subjects affected / exposed	1 / 178 (0.56%)	0 / 179 (0.00%)	0 / 53 (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
Mental status changes			
subjects affected / exposed	1 / 178 (0.56%)	0 / 179 (0.00%)	0 / 53 (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
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 178 (0.00%)	1 / 179 (0.56%)	0 / 53 (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
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 178 (0.00%)	1 / 179 (0.56%)	0 / 53 (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

Hepatic enzyme increased			
subjects affected / exposed	0 / 178 (0.00%)	1 / 179 (0.56%)	0 / 53 (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
Neutrophil count decreased			
subjects affected / exposed	0 / 178 (0.00%)	0 / 179 (0.00%)	0 / 53 (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
Platelet count decreased			
subjects affected / exposed	0 / 178 (0.00%)	0 / 179 (0.00%)	0 / 53 (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
White blood cell count decreased			
subjects affected / exposed	0 / 178 (0.00%)	0 / 179 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	1 / 178 (0.56%)	0 / 179 (0.00%)	0 / 53 (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
Femur fracture			
subjects affected / exposed	0 / 178 (0.00%)	0 / 179 (0.00%)	0 / 53 (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
Fracture displacement			
subjects affected / exposed	1 / 178 (0.56%)	0 / 179 (0.00%)	0 / 53 (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
Hip fracture			
subjects affected / exposed	1 / 178 (0.56%)	0 / 179 (0.00%)	0 / 53 (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

Lower limb fracture			
subjects affected / exposed	1 / 178 (0.56%)	0 / 179 (0.00%)	0 / 53 (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
Rib fracture			
subjects affected / exposed	1 / 178 (0.56%)	0 / 179 (0.00%)	0 / 53 (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	0 / 178 (0.00%)	1 / 179 (0.56%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subdural haematoma			
subjects affected / exposed	0 / 178 (0.00%)	0 / 179 (0.00%)	0 / 53 (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
Traumatic intracranial haemorrhage			
subjects affected / exposed	1 / 178 (0.56%)	0 / 179 (0.00%)	0 / 53 (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
Wound			
subjects affected / exposed	1 / 178 (0.56%)	0 / 179 (0.00%)	0 / 53 (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	0 / 178 (0.00%)	0 / 179 (0.00%)	1 / 53 (1.89%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	1 / 178 (0.56%)	0 / 179 (0.00%)	0 / 53 (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
Atrioventricular block complete			

subjects affected / exposed	1 / 178 (0.56%)	0 / 179 (0.00%)	0 / 53 (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 failure			
subjects affected / exposed	0 / 178 (0.00%)	1 / 179 (0.56%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac ventricular disorder			
subjects affected / exposed	0 / 178 (0.00%)	1 / 179 (0.56%)	0 / 53 (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
Cardiogenic shock			
subjects affected / exposed	1 / 178 (0.56%)	0 / 179 (0.00%)	0 / 53 (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
Myocardial infarction			
subjects affected / exposed	0 / 178 (0.00%)	0 / 179 (0.00%)	0 / 53 (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
Pericardial effusion			
subjects affected / exposed	1 / 178 (0.56%)	0 / 179 (0.00%)	0 / 53 (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
Nervous system disorders			
Ataxia			
subjects affected / exposed	0 / 178 (0.00%)	0 / 179 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrovascular accident			
subjects affected / exposed	1 / 178 (0.56%)	1 / 179 (0.56%)	0 / 53 (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
Dizziness			

subjects affected / exposed	0 / 178 (0.00%)	1 / 179 (0.56%)	1 / 53 (1.89%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Encephalopathy			
subjects affected / exposed	1 / 178 (0.56%)	0 / 179 (0.00%)	0 / 53 (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
Epilepsy			
subjects affected / exposed	2 / 178 (1.12%)	0 / 179 (0.00%)	0 / 53 (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
Haemorrhage intracranial			
subjects affected / exposed	0 / 178 (0.00%)	0 / 179 (0.00%)	0 / 53 (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
Hemiparesis			
subjects affected / exposed	0 / 178 (0.00%)	1 / 179 (0.56%)	0 / 53 (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
Hemiplegia			
subjects affected / exposed	1 / 178 (0.56%)	0 / 179 (0.00%)	0 / 53 (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
Lumbar radiculopathy			
subjects affected / exposed	0 / 178 (0.00%)	1 / 179 (0.56%)	0 / 53 (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
Meningitis noninfective			
subjects affected / exposed	0 / 178 (0.00%)	1 / 179 (0.56%)	0 / 53 (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
Myasthenic syndrome			

subjects affected / exposed	0 / 178 (0.00%)	1 / 179 (0.56%)	0 / 53 (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
Myoclonus			
subjects affected / exposed	0 / 178 (0.00%)	0 / 179 (0.00%)	0 / 53 (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
Neuropathy peripheral			
subjects affected / exposed	0 / 178 (0.00%)	1 / 179 (0.56%)	0 / 53 (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
Paraesthesia			
subjects affected / exposed	1 / 178 (0.56%)	0 / 179 (0.00%)	0 / 53 (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
Partial seizures			
subjects affected / exposed	2 / 178 (1.12%)	0 / 179 (0.00%)	0 / 53 (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
Presyncope			
subjects affected / exposed	1 / 178 (0.56%)	0 / 179 (0.00%)	0 / 53 (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
Sciatica			
subjects affected / exposed	0 / 178 (0.00%)	1 / 179 (0.56%)	0 / 53 (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
Seizure			
subjects affected / exposed	1 / 178 (0.56%)	0 / 179 (0.00%)	1 / 53 (1.89%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal cord compression			

subjects affected / exposed	1 / 178 (0.56%)	0 / 179 (0.00%)	0 / 53 (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	2 / 178 (1.12%)	0 / 179 (0.00%)	0 / 53 (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
Transient ischaemic attack			
subjects affected / exposed	0 / 178 (0.00%)	1 / 179 (0.56%)	0 / 53 (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
Depressed level of consciousness			
subjects affected / exposed	0 / 178 (0.00%)	0 / 179 (0.00%)	1 / 53 (1.89%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral motor neuropathy			
subjects affected / exposed	0 / 178 (0.00%)	0 / 179 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	7 / 178 (3.93%)	0 / 179 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	2 / 7	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bone marrow failure			
subjects affected / exposed	1 / 178 (0.56%)	0 / 179 (0.00%)	0 / 53 (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
Febrile neutropenia			
subjects affected / exposed	0 / 178 (0.00%)	0 / 179 (0.00%)	0 / 53 (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
Leukopenia			

subjects affected / exposed	0 / 178 (0.00%)	0 / 179 (0.00%)	0 / 53 (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
Neutropenia			
subjects affected / exposed	0 / 178 (0.00%)	0 / 179 (0.00%)	0 / 53 (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
Thrombocytopenia			
subjects affected / exposed	0 / 178 (0.00%)	0 / 179 (0.00%)	0 / 53 (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
Ear and labyrinth disorders			
Vertigo positional			
subjects affected / exposed	1 / 178 (0.56%)	0 / 179 (0.00%)	0 / 53 (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
Eye disorders			
Eye movement disorder			
subjects affected / exposed	1 / 178 (0.56%)	0 / 179 (0.00%)	0 / 53 (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
Iritis			
subjects affected / exposed	0 / 178 (0.00%)	1 / 179 (0.56%)	0 / 53 (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
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	2 / 178 (1.12%)	4 / 179 (2.23%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 2	1 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ascites			
subjects affected / exposed	0 / 178 (0.00%)	0 / 179 (0.00%)	0 / 53 (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

Autoimmune colitis			
subjects affected / exposed	1 / 178 (0.56%)	0 / 179 (0.00%)	0 / 53 (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	2 / 178 (1.12%)	2 / 179 (1.12%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	1 / 2	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Constipation			
subjects affected / exposed	2 / 178 (1.12%)	1 / 179 (0.56%)	0 / 53 (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
Diarrhoea			
subjects affected / exposed	1 / 178 (0.56%)	4 / 179 (2.23%)	1 / 53 (1.89%)
occurrences causally related to treatment / all	0 / 1	5 / 5	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulum			
subjects affected / exposed	1 / 178 (0.56%)	0 / 179 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dysphagia			
subjects affected / exposed	1 / 178 (0.56%)	0 / 179 (0.00%)	1 / 53 (1.89%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric disorder			
subjects affected / exposed	0 / 178 (0.00%)	1 / 179 (0.56%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorder			
subjects affected / exposed	0 / 178 (0.00%)	1 / 179 (0.56%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal pain			

subjects affected / exposed	1 / 178 (0.56%)	0 / 179 (0.00%)	0 / 53 (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
Haematemesis			
subjects affected / exposed	1 / 178 (0.56%)	0 / 179 (0.00%)	0 / 53 (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
Haematochezia			
subjects affected / exposed	0 / 178 (0.00%)	0 / 179 (0.00%)	0 / 53 (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
Ileus			
subjects affected / exposed	1 / 178 (0.56%)	2 / 179 (1.12%)	0 / 53 (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
Intestinal obstruction			
subjects affected / exposed	1 / 178 (0.56%)	0 / 179 (0.00%)	0 / 53 (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
Intussusception			
subjects affected / exposed	1 / 178 (0.56%)	0 / 179 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestinal ulcer			
subjects affected / exposed	1 / 178 (0.56%)	0 / 179 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestine perforation			
subjects affected / exposed	1 / 178 (0.56%)	0 / 179 (0.00%)	0 / 53 (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
Malabsorption			

subjects affected / exposed	1 / 178 (0.56%)	0 / 179 (0.00%)	0 / 53 (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
Nausea			
subjects affected / exposed	1 / 178 (0.56%)	0 / 179 (0.00%)	0 / 53 (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
Odynophagia			
subjects affected / exposed	0 / 178 (0.00%)	1 / 179 (0.56%)	0 / 53 (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
Pancreatitis			
subjects affected / exposed	1 / 178 (0.56%)	1 / 179 (0.56%)	1 / 53 (1.89%)
occurrences causally related to treatment / all	1 / 1	3 / 3	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal haemorrhage			
subjects affected / exposed	0 / 178 (0.00%)	0 / 179 (0.00%)	0 / 53 (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
Small intestinal obstruction			
subjects affected / exposed	0 / 178 (0.00%)	1 / 179 (0.56%)	0 / 53 (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
Small intestinal perforation			
subjects affected / exposed	1 / 178 (0.56%)	0 / 179 (0.00%)	0 / 53 (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
Upper gastrointestinal haemorrhage			
subjects affected / exposed	1 / 178 (0.56%)	1 / 179 (0.56%)	0 / 53 (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
Vomiting			

subjects affected / exposed	3 / 178 (1.69%)	1 / 179 (0.56%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower gastrointestinal haemorrhage			
subjects affected / exposed	0 / 178 (0.00%)	0 / 179 (0.00%)	0 / 53 (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
Hepatobiliary disorders			
Autoimmune hepatitis			
subjects affected / exposed	0 / 178 (0.00%)	1 / 179 (0.56%)	0 / 53 (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
Cholangitis			
subjects affected / exposed	0 / 178 (0.00%)	1 / 179 (0.56%)	0 / 53 (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
Cholecystitis			
subjects affected / exposed	2 / 178 (1.12%)	0 / 179 (0.00%)	0 / 53 (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
Hepatic failure			
subjects affected / exposed	1 / 178 (0.56%)	1 / 179 (0.56%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 0
Hepatic necrosis			
subjects affected / exposed	0 / 178 (0.00%)	0 / 179 (0.00%)	0 / 53 (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
Hyperbilirubinaemia			
subjects affected / exposed	0 / 178 (0.00%)	0 / 179 (0.00%)	0 / 53 (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
Bile duct obstruction			

subjects affected / exposed	0 / 178 (0.00%)	0 / 179 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Lichenoid keratosis			
subjects affected / exposed	0 / 178 (0.00%)	1 / 179 (0.56%)	0 / 53 (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 maculo-papular			
subjects affected / exposed	1 / 178 (0.56%)	0 / 179 (0.00%)	0 / 53 (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
Skin mass			
subjects affected / exposed	1 / 178 (0.56%)	0 / 179 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stevens-Johnson syndrome			
subjects affected / exposed	1 / 178 (0.56%)	0 / 179 (0.00%)	0 / 53 (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
Purpura			
subjects affected / exposed	0 / 178 (0.00%)	0 / 179 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 178 (0.56%)	1 / 179 (0.56%)	0 / 53 (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
Hydronephrosis			
subjects affected / exposed	1 / 178 (0.56%)	0 / 179 (0.00%)	0 / 53 (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
Obstructive uropathy			

subjects affected / exposed	0 / 178 (0.00%)	1 / 179 (0.56%)	0 / 53 (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
Postrenal failure			
subjects affected / exposed	1 / 178 (0.56%)	0 / 179 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal failure			
subjects affected / exposed	1 / 178 (0.56%)	0 / 179 (0.00%)	0 / 53 (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
Tubulointerstitial nephritis			
subjects affected / exposed	1 / 178 (0.56%)	0 / 179 (0.00%)	0 / 53 (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 impairment			
subjects affected / exposed	0 / 178 (0.00%)	0 / 179 (0.00%)	0 / 53 (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
Endocrine disorders			
Addison's disease			
subjects affected / exposed	0 / 178 (0.00%)	0 / 179 (0.00%)	0 / 53 (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
Adrenal insufficiency			
subjects affected / exposed	1 / 178 (0.56%)	0 / 179 (0.00%)	0 / 53 (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
Adrenocortical insufficiency acute			
subjects affected / exposed	0 / 178 (0.00%)	1 / 179 (0.56%)	0 / 53 (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
Hyperparathyroidism			

subjects affected / exposed	0 / 178 (0.00%)	1 / 179 (0.56%)	0 / 53 (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
Hypophysitis			
subjects affected / exposed	1 / 178 (0.56%)	0 / 179 (0.00%)	0 / 53 (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
Hypopituitarism			
subjects affected / exposed	0 / 178 (0.00%)	2 / 179 (1.12%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Secondary adrenocortical insufficiency			
subjects affected / exposed	0 / 178 (0.00%)	1 / 179 (0.56%)	0 / 53 (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
Inappropriate antidiuretic hormone secretion			
subjects affected / exposed	0 / 178 (0.00%)	0 / 179 (0.00%)	1 / 53 (1.89%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 178 (0.00%)	2 / 179 (1.12%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Back pain			
subjects affected / exposed	0 / 178 (0.00%)	2 / 179 (1.12%)	0 / 53 (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
Groin pain			
subjects affected / exposed	0 / 178 (0.00%)	1 / 179 (0.56%)	0 / 53 (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	0 / 178 (0.00%)	1 / 179 (0.56%)	0 / 53 (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
Musculoskeletal pain			
subjects affected / exposed	1 / 178 (0.56%)	1 / 179 (0.56%)	0 / 53 (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
Neck pain			
subjects affected / exposed	0 / 178 (0.00%)	1 / 179 (0.56%)	0 / 53 (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	0 / 178 (0.00%)	1 / 179 (0.56%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain in extremity			
subjects affected / exposed	0 / 178 (0.00%)	0 / 179 (0.00%)	0 / 53 (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
Spondylolisthesis			
subjects affected / exposed	0 / 178 (0.00%)	1 / 179 (0.56%)	0 / 53 (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
Cervical spinal stenosis			
subjects affected / exposed	0 / 178 (0.00%)	0 / 179 (0.00%)	1 / 53 (1.89%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Appendicitis perforated			
subjects affected / exposed	0 / 178 (0.00%)	1 / 179 (0.56%)	0 / 53 (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
Atypical pneumonia			

subjects affected / exposed	0 / 178 (0.00%)	0 / 179 (0.00%)	0 / 53 (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
Bacteraemia			
subjects affected / exposed	0 / 178 (0.00%)	0 / 179 (0.00%)	0 / 53 (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
Bronchitis			
subjects affected / exposed	2 / 178 (1.12%)	0 / 179 (0.00%)	0 / 53 (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
Candida infection			
subjects affected / exposed	0 / 178 (0.00%)	1 / 179 (0.56%)	0 / 53 (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	1 / 178 (0.56%)	0 / 179 (0.00%)	0 / 53 (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
Cellulitis streptococcal			
subjects affected / exposed	1 / 178 (0.56%)	0 / 179 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium difficile colitis			
subjects affected / exposed	1 / 178 (0.56%)	0 / 179 (0.00%)	0 / 53 (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 / 178 (0.56%)	0 / 179 (0.00%)	0 / 53 (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
Enterocolitis infectious			

subjects affected / exposed	0 / 178 (0.00%)	0 / 179 (0.00%)	0 / 53 (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
Erysipelas			
subjects affected / exposed	2 / 178 (1.12%)	1 / 179 (0.56%)	0 / 53 (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
Gastroenteritis viral			
subjects affected / exposed	0 / 178 (0.00%)	1 / 179 (0.56%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes zoster			
subjects affected / exposed	0 / 178 (0.00%)	1 / 179 (0.56%)	0 / 53 (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
Infected cyst			
subjects affected / exposed	0 / 178 (0.00%)	1 / 179 (0.56%)	0 / 53 (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	0 / 178 (0.00%)	0 / 179 (0.00%)	0 / 53 (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
Infectious pleural effusion			
subjects affected / exposed	1 / 178 (0.56%)	0 / 179 (0.00%)	0 / 53 (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
Influenza			
subjects affected / exposed	0 / 178 (0.00%)	1 / 179 (0.56%)	0 / 53 (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
Mastitis			

subjects affected / exposed	1 / 178 (0.56%)	0 / 179 (0.00%)	0 / 53 (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
Osteomyelitis			
subjects affected / exposed	0 / 178 (0.00%)	1 / 179 (0.56%)	0 / 53 (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
Pelvic abscess			
subjects affected / exposed	0 / 178 (0.00%)	1 / 179 (0.56%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	3 / 178 (1.69%)	3 / 179 (1.68%)	3 / 53 (5.66%)
occurrences causally related to treatment / all	0 / 3	2 / 5	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory syncytial virus infection			
subjects affected / exposed	0 / 178 (0.00%)	0 / 179 (0.00%)	0 / 53 (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
Salmonellosis			
subjects affected / exposed	0 / 178 (0.00%)	1 / 179 (0.56%)	0 / 53 (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	1 / 178 (0.56%)	1 / 179 (0.56%)	0 / 53 (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
Septic shock			
subjects affected / exposed	1 / 178 (0.56%)	0 / 179 (0.00%)	0 / 53 (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
Skin infection			

subjects affected / exposed	2 / 178 (1.12%)	0 / 179 (0.00%)	0 / 53 (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
Soft tissue infection			
subjects affected / exposed	1 / 178 (0.56%)	0 / 179 (0.00%)	0 / 53 (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
Streptococcal sepsis			
subjects affected / exposed	1 / 178 (0.56%)	0 / 179 (0.00%)	0 / 53 (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	2 / 178 (1.12%)	1 / 179 (0.56%)	0 / 53 (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
Viral infection			
subjects affected / exposed	1 / 178 (0.56%)	0 / 179 (0.00%)	0 / 53 (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
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 178 (0.00%)	0 / 179 (0.00%)	0 / 53 (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
Wound infection			
subjects affected / exposed	1 / 178 (0.56%)	0 / 179 (0.00%)	0 / 53 (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
Lung infection			
subjects affected / exposed	0 / 178 (0.00%)	0 / 179 (0.00%)	1 / 53 (1.89%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Postoperative wound infection			

subjects affected / exposed	0 / 178 (0.00%)	0 / 179 (0.00%)	0 / 53 (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
Urosepsis			
subjects affected / exposed	0 / 178 (0.00%)	0 / 179 (0.00%)	1 / 53 (1.89%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Cachexia			
subjects affected / exposed	1 / 178 (0.56%)	0 / 179 (0.00%)	1 / 53 (1.89%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
Dehydration			
subjects affected / exposed	5 / 178 (2.81%)	1 / 179 (0.56%)	0 / 53 (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
Diabetic metabolic decompensation			
subjects affected / exposed	1 / 178 (0.56%)	0 / 179 (0.00%)	0 / 53 (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	1 / 178 (0.56%)	0 / 179 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperglycaemia			
subjects affected / exposed	1 / 178 (0.56%)	0 / 179 (0.00%)	0 / 53 (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
Hypocalcaemia			
subjects affected / exposed	0 / 178 (0.00%)	0 / 179 (0.00%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemia			

subjects affected / exposed	1 / 178 (0.56%)	3 / 179 (1.68%)	0 / 53 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	ICC (After Switch to Pembrolizumab 10 mg/kg)		
Total subjects affected by serious adverse events			
subjects affected / exposed	18 / 45 (40.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	0 / 45 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cancer pain			
subjects affected / exposed	0 / 45 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Colon cancer metastatic			
subjects affected / exposed	0 / 45 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Intracranial tumour haemorrhage			
subjects affected / exposed	0 / 45 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Invasive ductal breast carcinoma			
subjects affected / exposed	0 / 45 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metastases to central nervous system			

subjects affected / exposed	1 / 45 (2.22%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Metastases to lymph nodes				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Metastases to small intestine				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Metastatic pain				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Oncologic complication				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Prostate cancer				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Rectal cancer				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Squamous cell carcinoma of skin				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Tumour haemorrhage				

subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Tumour pain				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vascular disorders				
Circulatory collapse				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Deep vein thrombosis				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Haemorrhagic infarction				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypotension				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lymphoedema				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Orthostatic hypotension				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Phlebitis				

subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Poor venous access				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Venous thrombosis				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Thrombosis				
subjects affected / exposed	1 / 45 (2.22%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
General disorders and administration site conditions				
Asthenia				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Chest pain				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cyst				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Death				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Device dislocation				

subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Fatigue				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gait disturbance				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
General physical health deterioration				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Generalised oedema				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Infusion site extravasation				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Malaise				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Oedema				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pyrexia				

subjects affected / exposed	0 / 45 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	0 / 45 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypersensitivity			
subjects affected / exposed	0 / 45 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cytokine release syndrome			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Pelvic pain			
subjects affected / exposed	0 / 45 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 45 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cough			
subjects affected / exposed	0 / 45 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Dyspnoea			

subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Dyspnoea exertional				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Epistaxis				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Haemoptysis				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Haemothorax				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypoxia				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Interstitial lung disease				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Laryngeal inflammation				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pleural effusion				

subjects affected / exposed	1 / 45 (2.22%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia aspiration				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonitis				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumothorax				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pulmonary embolism				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pulmonary thrombosis				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Acute respiratory failure				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Alveolitis allergic				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Psychiatric disorders				
Confusional state				

subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Delirium				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Mental status changes				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Investigations				
Alanine aminotransferase increased				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Aspartate aminotransferase increased				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hepatic enzyme increased				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Neutrophil count decreased				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Platelet count decreased				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
White blood cell count decreased				

subjects affected / exposed	0 / 45 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 45 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Femur fracture			
subjects affected / exposed	0 / 45 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Fracture displacement			
subjects affected / exposed	0 / 45 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hip fracture			
subjects affected / exposed	0 / 45 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Lower limb fracture			
subjects affected / exposed	0 / 45 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Rib fracture			
subjects affected / exposed	0 / 45 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Spinal fracture			
subjects affected / exposed	0 / 45 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Subdural haematoma			

subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Traumatic intracranial haemorrhage				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Wound				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Accidental overdose				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
Atrial fibrillation				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Atrioventricular block complete				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac failure				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac ventricular disorder				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiogenic shock				

subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Myocardial infarction				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pericardial effusion				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
Ataxia				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cerebrovascular accident				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Dizziness				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Encephalopathy				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Epilepsy				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Haemorrhage intracranial				

subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hemiparesis				
subjects affected / exposed	1 / 45 (2.22%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hemiplegia				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lumbar radiculopathy				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Meningitis noninfective				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Myasthenic syndrome				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Myoclonus				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Neuropathy peripheral				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Paraesthesia				

subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Partial seizures				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Presyncope				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Sciatica				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Seizure				
subjects affected / exposed	2 / 45 (4.44%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Spinal cord compression				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Syncope				
subjects affected / exposed	1 / 45 (2.22%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Transient ischaemic attack				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Depressed level of consciousness				

subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Peripheral motor neuropathy				
subjects affected / exposed	1 / 45 (2.22%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Blood and lymphatic system disorders				
Anaemia				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bone marrow failure				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Febrile neutropenia				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Leukopenia				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Neutropenia				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Thrombocytopenia				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ear and labyrinth disorders				

Vertigo positional			
subjects affected / exposed	0 / 45 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Eye movement disorder			
subjects affected / exposed	0 / 45 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Iritis			
subjects affected / exposed	0 / 45 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 45 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Ascites			
subjects affected / exposed	0 / 45 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Autoimmune colitis			
subjects affected / exposed	0 / 45 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Colitis			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Constipation			
subjects affected / exposed	0 / 45 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Diarrhoea				
subjects affected / exposed	1 / 45 (2.22%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Diverticulum				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Dysphagia				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastric disorder				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorder				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal pain				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Haematemesis				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Haematochezia				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ileus				

subjects affected / exposed	0 / 45 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Intestinal obstruction			
subjects affected / exposed	0 / 45 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Intussusception			
subjects affected / exposed	0 / 45 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Large intestinal ulcer			
subjects affected / exposed	0 / 45 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Large intestine perforation			
subjects affected / exposed	0 / 45 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Malabsorption			
subjects affected / exposed	0 / 45 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nausea			
subjects affected / exposed	0 / 45 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Odynophagia			
subjects affected / exposed	0 / 45 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pancreatitis			

subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Rectal haemorrhage				
subjects affected / exposed	1 / 45 (2.22%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Small intestinal obstruction				
subjects affected / exposed	1 / 45 (2.22%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Small intestinal perforation				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Upper gastrointestinal haemorrhage				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vomiting				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lower gastrointestinal haemorrhage				
subjects affected / exposed	2 / 45 (4.44%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Hepatobiliary disorders				
Autoimmune hepatitis				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cholangitis				

subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cholecystitis				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hepatic failure				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hepatic necrosis				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hyperbilirubinaemia				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bile duct obstruction				
subjects affected / exposed	1 / 45 (2.22%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Skin and subcutaneous tissue disorders				
Lichenoid keratosis				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Rash maculo-papular				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Skin mass				

subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Stevens-Johnson syndrome				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Purpura				
subjects affected / exposed	1 / 45 (2.22%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Renal and urinary disorders				
Acute kidney injury				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hydronephrosis				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Obstructive uropathy				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Postrenal failure				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Renal failure				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Tubulointerstitial nephritis				

subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Renal impairment				
subjects affected / exposed	1 / 45 (2.22%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Endocrine disorders				
Addison's disease				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Adrenal insufficiency				
subjects affected / exposed	1 / 45 (2.22%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Adrenocortical insufficiency acute				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hyperparathyroidism				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypophysitis				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypopituitarism				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Secondary adrenocortical insufficiency				

subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Inappropriate antidiuretic hormone secretion				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal and connective tissue disorders				
Arthralgia				
subjects affected / exposed	1 / 45 (2.22%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Back pain				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Groin pain				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Muscular weakness				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal pain				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Neck pain				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Osteolysis				

subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pain in extremity				
subjects affected / exposed	1 / 45 (2.22%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Spondylolisthesis				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cervical spinal stenosis				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Appendicitis perforated				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Atypical pneumonia				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bacteraemia				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bronchitis				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Candida infection				

subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cellulitis				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cellulitis streptococcal				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Clostridium difficile colitis				
subjects affected / exposed	1 / 45 (2.22%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Diverticulitis				
subjects affected / exposed	1 / 45 (2.22%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Enterocolitis infectious				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Erysipelas				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis viral				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Herpes zoster				

subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Infected cyst				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Infection				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Infectious pleural effusion				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Influenza				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Mastitis				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Osteomyelitis				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pelvic abscess				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia				

subjects affected / exposed	1 / 45 (2.22%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory syncytial virus infection				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Salmonellosis				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Sepsis				
subjects affected / exposed	1 / 45 (2.22%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Septic shock				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Skin infection				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Soft tissue infection				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Streptococcal sepsis				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Urinary tract infection				

subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Viral infection				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Viral upper respiratory tract infection				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Wound infection				
subjects affected / exposed	1 / 45 (2.22%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Lung infection				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Postoperative wound infection				
subjects affected / exposed	1 / 45 (2.22%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Urosepsis				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Metabolism and nutrition disorders				
Cachexia				
subjects affected / exposed	0 / 45 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Dehydration				

subjects affected / exposed	0 / 45 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Diabetic metabolic decompensation			
subjects affected / exposed	0 / 45 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypercalcaemia			
subjects affected / exposed	0 / 45 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hyperglycaemia			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hypocalcaemia			
subjects affected / exposed	0 / 45 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hyponatraemia			
subjects affected / exposed	0 / 45 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	ICC (Before Switch to Pembrolizumab 10 mg/kg)	ICC Only	ICC (Before Switch to Pembrolizumab 2 mg/kg)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	44 / 45 (97.78%)	66 / 73 (90.41%)	52 / 53 (98.11%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour pain			
subjects affected / exposed	3 / 45 (6.67%)	4 / 73 (5.48%)	4 / 53 (7.55%)
occurrences (all)	3	4	4

Melanocytic naevus			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 45 (0.00%)	1 / 73 (1.37%)	0 / 53 (0.00%)
occurrences (all)	0	1	0
Deep vein thrombosis			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	2 / 45 (4.44%)	10 / 73 (13.70%)	4 / 53 (7.55%)
occurrences (all)	2	11	4
Chest pain			
subjects affected / exposed	1 / 45 (2.22%)	3 / 73 (4.11%)	3 / 53 (5.66%)
occurrences (all)	1	3	4
Chills			
subjects affected / exposed	5 / 45 (11.11%)	0 / 73 (0.00%)	3 / 53 (5.66%)
occurrences (all)	5	0	3
Fatigue			
subjects affected / exposed	26 / 45 (57.78%)	28 / 73 (38.36%)	27 / 53 (50.94%)
occurrences (all)	33	34	36
Influenza like illness			
subjects affected / exposed	1 / 45 (2.22%)	1 / 73 (1.37%)	1 / 53 (1.89%)
occurrences (all)	1	2	1
Malaise			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	3 / 53 (5.66%)
occurrences (all)	0	0	3
Oedema peripheral			
subjects affected / exposed	1 / 45 (2.22%)	4 / 73 (5.48%)	5 / 53 (9.43%)
occurrences (all)	1	4	5
Pain			
subjects affected / exposed	1 / 45 (2.22%)	0 / 73 (0.00%)	4 / 53 (7.55%)
occurrences (all)	1	0	5
Pyrexia			

subjects affected / exposed	5 / 45 (11.11%)	7 / 73 (9.59%)	5 / 53 (9.43%)
occurrences (all)	6	7	7
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	6 / 45 (13.33%)	9 / 73 (12.33%)	13 / 53 (24.53%)
occurrences (all)	8	9	13
Dyspnoea			
subjects affected / exposed	1 / 45 (2.22%)	9 / 73 (12.33%)	10 / 53 (18.87%)
occurrences (all)	1	10	10
Pleural effusion			
subjects affected / exposed	0 / 45 (0.00%)	4 / 73 (5.48%)	1 / 53 (1.89%)
occurrences (all)	0	4	1
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 45 (2.22%)	4 / 73 (5.48%)	4 / 53 (7.55%)
occurrences (all)	1	6	4
Depression			
subjects affected / exposed	1 / 45 (2.22%)	4 / 73 (5.48%)	4 / 53 (7.55%)
occurrences (all)	1	4	4
Insomnia			
subjects affected / exposed	3 / 45 (6.67%)	8 / 73 (10.96%)	2 / 53 (3.77%)
occurrences (all)	3	8	2
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	3 / 45 (6.67%)	0 / 73 (0.00%)	2 / 53 (3.77%)
occurrences (all)	4	0	2
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 45 (2.22%)	0 / 73 (0.00%)	1 / 53 (1.89%)
occurrences (all)	1	0	2
Blood alkaline phosphatase increased			
subjects affected / exposed	2 / 45 (4.44%)	2 / 73 (2.74%)	1 / 53 (1.89%)
occurrences (all)	2	2	1
Blood bilirubin increased			
subjects affected / exposed	0 / 45 (0.00%)	1 / 73 (1.37%)	3 / 53 (5.66%)
occurrences (all)	0	1	3
Blood cholesterol increased			

subjects affected / exposed	3 / 45 (6.67%)	0 / 73 (0.00%)	2 / 53 (3.77%)
occurrences (all)	3	0	2
Lymphocyte count decreased			
subjects affected / exposed	2 / 45 (4.44%)	4 / 73 (5.48%)	3 / 53 (5.66%)
occurrences (all)	2	4	4
Neutrophil count decreased			
subjects affected / exposed	4 / 45 (8.89%)	3 / 73 (4.11%)	3 / 53 (5.66%)
occurrences (all)	5	3	4
Platelet count decreased			
subjects affected / exposed	5 / 45 (11.11%)	5 / 73 (6.85%)	4 / 53 (7.55%)
occurrences (all)	8	7	9
Weight decreased			
subjects affected / exposed	3 / 45 (6.67%)	1 / 73 (1.37%)	4 / 53 (7.55%)
occurrences (all)	3	1	5
White blood cell count decreased			
subjects affected / exposed	3 / 45 (6.67%)	5 / 73 (6.85%)	3 / 53 (5.66%)
occurrences (all)	3	6	3
Blood creatinine increased			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Tachycardia			
subjects affected / exposed	0 / 45 (0.00%)	4 / 73 (5.48%)	2 / 53 (3.77%)
occurrences (all)	0	4	3
Nervous system disorders			
Dizziness			
subjects affected / exposed	3 / 45 (6.67%)	9 / 73 (12.33%)	4 / 53 (7.55%)
occurrences (all)	3	9	4
Dysgeusia			
subjects affected / exposed	4 / 45 (8.89%)	2 / 73 (2.74%)	5 / 53 (9.43%)
occurrences (all)	4	2	5
Headache			
subjects affected / exposed	7 / 45 (15.56%)	8 / 73 (10.96%)	9 / 53 (16.98%)
occurrences (all)	10	8	11
Neuropathy peripheral			

subjects affected / exposed	5 / 45 (11.11%)	6 / 73 (8.22%)	7 / 53 (13.21%)
occurrences (all)	7	6	7
Paraesthesia			
subjects affected / exposed	3 / 45 (6.67%)	3 / 73 (4.11%)	5 / 53 (9.43%)
occurrences (all)	3	3	6
Tremor			
subjects affected / exposed	3 / 45 (6.67%)	0 / 73 (0.00%)	1 / 53 (1.89%)
occurrences (all)	3	0	1
Peripheral sensory neuropathy			
subjects affected / exposed	3 / 45 (6.67%)	1 / 73 (1.37%)	2 / 53 (3.77%)
occurrences (all)	3	1	2
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	10 / 45 (22.22%)	21 / 73 (28.77%)	15 / 53 (28.30%)
occurrences (all)	10	26	25
Leukopenia			
subjects affected / exposed	4 / 45 (8.89%)	8 / 73 (10.96%)	3 / 53 (5.66%)
occurrences (all)	7	8	6
Neutropenia			
subjects affected / exposed	5 / 45 (11.11%)	2 / 73 (2.74%)	7 / 53 (13.21%)
occurrences (all)	8	2	14
Thrombocytopenia			
subjects affected / exposed	2 / 45 (4.44%)	9 / 73 (12.33%)	7 / 53 (13.21%)
occurrences (all)	2	12	10
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 45 (0.00%)	3 / 73 (4.11%)	1 / 53 (1.89%)
occurrences (all)	0	3	1
Eye disorders			
Dry eye			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	0 / 45 (0.00%)	1 / 73 (1.37%)	3 / 53 (5.66%)
occurrences (all)	0	1	3
Abdominal pain			

subjects affected / exposed	4 / 45 (8.89%)	8 / 73 (10.96%)	1 / 53 (1.89%)
occurrences (all)	4	10	2
Abdominal pain upper			
subjects affected / exposed	2 / 45 (4.44%)	2 / 73 (2.74%)	1 / 53 (1.89%)
occurrences (all)	2	2	1
Constipation			
subjects affected / exposed	8 / 45 (17.78%)	16 / 73 (21.92%)	12 / 53 (22.64%)
occurrences (all)	10	19	17
Diarrhoea			
subjects affected / exposed	11 / 45 (24.44%)	13 / 73 (17.81%)	11 / 53 (20.75%)
occurrences (all)	17	20	17
Dry mouth			
subjects affected / exposed	0 / 45 (0.00%)	1 / 73 (1.37%)	0 / 53 (0.00%)
occurrences (all)	0	1	0
Dyspepsia			
subjects affected / exposed	3 / 45 (6.67%)	2 / 73 (2.74%)	2 / 53 (3.77%)
occurrences (all)	3	2	3
Nausea			
subjects affected / exposed	19 / 45 (42.22%)	23 / 73 (31.51%)	29 / 53 (54.72%)
occurrences (all)	23	30	44
Vomiting			
subjects affected / exposed	13 / 45 (28.89%)	17 / 73 (23.29%)	10 / 53 (18.87%)
occurrences (all)	14	22	14
Dysphagia			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	11 / 45 (24.44%)	10 / 73 (13.70%)	16 / 53 (30.19%)
occurrences (all)	11	10	19
Dry skin			
subjects affected / exposed	0 / 45 (0.00%)	4 / 73 (5.48%)	1 / 53 (1.89%)
occurrences (all)	0	4	1
Night sweats			
subjects affected / exposed	3 / 45 (6.67%)	2 / 73 (2.74%)	4 / 53 (7.55%)
occurrences (all)	4	2	5

Erythema			
subjects affected / exposed	1 / 45 (2.22%)	2 / 73 (2.74%)	2 / 53 (3.77%)
occurrences (all)	2	2	2
Pruritus			
subjects affected / exposed	6 / 45 (13.33%)	5 / 73 (6.85%)	4 / 53 (7.55%)
occurrences (all)	6	6	4
Rash			
subjects affected / exposed	3 / 45 (6.67%)	6 / 73 (8.22%)	4 / 53 (7.55%)
occurrences (all)	3	7	5
Rash maculo-papular			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (0.00%)
occurrences (all)	0	0	0
Vitiligo			
subjects affected / exposed	1 / 45 (2.22%)	0 / 73 (0.00%)	2 / 53 (3.77%)
occurrences (all)	1	0	2
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	1 / 45 (2.22%)	0 / 73 (0.00%)	0 / 53 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	7 / 45 (15.56%)	5 / 73 (6.85%)	6 / 53 (11.32%)
occurrences (all)	9	6	7
Back pain			
subjects affected / exposed	6 / 45 (13.33%)	8 / 73 (10.96%)	5 / 53 (9.43%)
occurrences (all)	6	10	5
Bone pain			
subjects affected / exposed	3 / 45 (6.67%)	1 / 73 (1.37%)	2 / 53 (3.77%)
occurrences (all)	3	1	10
Muscular weakness			
subjects affected / exposed	2 / 45 (4.44%)	3 / 73 (4.11%)	5 / 53 (9.43%)
occurrences (all)	3	3	6
Myalgia			
subjects affected / exposed	4 / 45 (8.89%)	3 / 73 (4.11%)	4 / 53 (7.55%)
occurrences (all)	7	3	4
Musculoskeletal pain			

subjects affected / exposed	1 / 45 (2.22%)	3 / 73 (4.11%)	4 / 53 (7.55%)
occurrences (all)	1	3	4
Pain in extremity			
subjects affected / exposed	5 / 45 (11.11%)	2 / 73 (2.74%)	6 / 53 (11.32%)
occurrences (all)	5	2	6
Muscle spasms			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (0.00%)
occurrences (all)	0	0	0
Neck pain			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	1 / 45 (2.22%)	2 / 73 (2.74%)	4 / 53 (7.55%)
occurrences (all)	1	2	4
Upper respiratory tract infection			
subjects affected / exposed	2 / 45 (4.44%)	1 / 73 (1.37%)	1 / 53 (1.89%)
occurrences (all)	2	1	2
Urinary tract infection			
subjects affected / exposed	2 / 45 (4.44%)	5 / 73 (6.85%)	2 / 53 (3.77%)
occurrences (all)	2	5	2
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	11 / 45 (24.44%)	20 / 73 (27.40%)	8 / 53 (15.09%)
occurrences (all)	12	21	10
Dehydration			
subjects affected / exposed	3 / 45 (6.67%)	2 / 73 (2.74%)	3 / 53 (5.66%)
occurrences (all)	4	3	7
Hyperglycaemia			
subjects affected / exposed	3 / 45 (6.67%)	2 / 73 (2.74%)	5 / 53 (9.43%)
occurrences (all)	3	2	10
Hypertriglyceridaemia			
subjects affected / exposed	5 / 45 (11.11%)	0 / 73 (0.00%)	4 / 53 (7.55%)
occurrences (all)	7	0	5
Hypoalbuminaemia			

subjects affected / exposed	2 / 45 (4.44%)	5 / 73 (6.85%)	3 / 53 (5.66%)
occurrences (all)	2	5	4
Hypokalaemia			
subjects affected / exposed	3 / 45 (6.67%)	3 / 73 (4.11%)	4 / 53 (7.55%)
occurrences (all)	3	3	5
Hyponatraemia			
subjects affected / exposed	2 / 45 (4.44%)	4 / 73 (5.48%)	3 / 53 (5.66%)
occurrences (all)	3	6	3
Hyperkalaemia			
subjects affected / exposed	0 / 45 (0.00%)	0 / 73 (0.00%)	0 / 53 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Pembrolizumab 2 mg/kg	Pembrolizumab 10 mg/kg	ICC (After Switch to Pembrolizumab 2 mg/kg)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	157 / 178 (88.20%)	176 / 179 (98.32%)	48 / 53 (90.57%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour pain			
subjects affected / exposed	2 / 178 (1.12%)	8 / 179 (4.47%)	0 / 53 (0.00%)
occurrences (all)	2	8	0
Melanocytic naevus			
subjects affected / exposed	0 / 178 (0.00%)	0 / 179 (0.00%)	3 / 53 (5.66%)
occurrences (all)	0	0	5
Vascular disorders			
Hypotension			
subjects affected / exposed	5 / 178 (2.81%)	10 / 179 (5.59%)	2 / 53 (3.77%)
occurrences (all)	7	10	2
Deep vein thrombosis			
subjects affected / exposed	0 / 178 (0.00%)	0 / 179 (0.00%)	3 / 53 (5.66%)
occurrences (all)	0	0	3
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	19 / 178 (10.67%)	20 / 179 (11.17%)	2 / 53 (3.77%)
occurrences (all)	25	30	2
Chest pain			

subjects affected / exposed	7 / 178 (3.93%)	11 / 179 (6.15%)	0 / 53 (0.00%)
occurrences (all)	8	14	0
Chills			
subjects affected / exposed	10 / 178 (5.62%)	11 / 179 (6.15%)	0 / 53 (0.00%)
occurrences (all)	11	13	0
Fatigue			
subjects affected / exposed	74 / 178 (41.57%)	91 / 179 (50.84%)	14 / 53 (26.42%)
occurrences (all)	106	114	14
Influenza like illness			
subjects affected / exposed	9 / 178 (5.06%)	12 / 179 (6.70%)	3 / 53 (5.66%)
occurrences (all)	12	15	3
Malaise			
subjects affected / exposed	7 / 178 (3.93%)	2 / 179 (1.12%)	0 / 53 (0.00%)
occurrences (all)	9	2	0
Oedema peripheral			
subjects affected / exposed	17 / 178 (9.55%)	21 / 179 (11.73%)	6 / 53 (11.32%)
occurrences (all)	19	24	7
Pain			
subjects affected / exposed	6 / 178 (3.37%)	7 / 179 (3.91%)	3 / 53 (5.66%)
occurrences (all)	7	7	3
Pyrexia			
subjects affected / exposed	23 / 178 (12.92%)	29 / 179 (16.20%)	3 / 53 (5.66%)
occurrences (all)	30	42	4
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	37 / 178 (20.79%)	36 / 179 (20.11%)	7 / 53 (13.21%)
occurrences (all)	48	45	7
Dyspnoea			
subjects affected / exposed	18 / 178 (10.11%)	29 / 179 (16.20%)	7 / 53 (13.21%)
occurrences (all)	20	33	7
Pleural effusion			
subjects affected / exposed	3 / 178 (1.69%)	3 / 179 (1.68%)	4 / 53 (7.55%)
occurrences (all)	3	3	4
Psychiatric disorders			

Anxiety			
subjects affected / exposed	10 / 178 (5.62%)	8 / 179 (4.47%)	3 / 53 (5.66%)
occurrences (all)	10	8	3
Depression			
subjects affected / exposed	6 / 178 (3.37%)	11 / 179 (6.15%)	0 / 53 (0.00%)
occurrences (all)	6	12	0
Insomnia			
subjects affected / exposed	9 / 178 (5.06%)	10 / 179 (5.59%)	0 / 53 (0.00%)
occurrences (all)	10	11	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	9 / 178 (5.06%)	12 / 179 (6.70%)	3 / 53 (5.66%)
occurrences (all)	10	17	4
Aspartate aminotransferase increased			
subjects affected / exposed	11 / 178 (6.18%)	13 / 179 (7.26%)	3 / 53 (5.66%)
occurrences (all)	11	16	4
Blood alkaline phosphatase increased			
subjects affected / exposed	12 / 178 (6.74%)	9 / 179 (5.03%)	3 / 53 (5.66%)
occurrences (all)	13	15	3
Blood bilirubin increased			
subjects affected / exposed	6 / 178 (3.37%)	2 / 179 (1.12%)	0 / 53 (0.00%)
occurrences (all)	10	5	0
Blood cholesterol increased			
subjects affected / exposed	5 / 178 (2.81%)	5 / 179 (2.79%)	0 / 53 (0.00%)
occurrences (all)	8	11	0
Lymphocyte count decreased			
subjects affected / exposed	6 / 178 (3.37%)	7 / 179 (3.91%)	0 / 53 (0.00%)
occurrences (all)	17	8	0
Neutrophil count decreased			
subjects affected / exposed	2 / 178 (1.12%)	1 / 179 (0.56%)	0 / 53 (0.00%)
occurrences (all)	9	1	0
Platelet count decreased			
subjects affected / exposed	2 / 178 (1.12%)	5 / 179 (2.79%)	0 / 53 (0.00%)
occurrences (all)	9	9	0
Weight decreased			

subjects affected / exposed	12 / 178 (6.74%)	17 / 179 (9.50%)	4 / 53 (7.55%)
occurrences (all)	12	17	5
White blood cell count decreased			
subjects affected / exposed	4 / 178 (2.25%)	2 / 179 (1.12%)	0 / 53 (0.00%)
occurrences (all)	11	2	0
Blood creatinine increased			
subjects affected / exposed	0 / 178 (0.00%)	0 / 179 (0.00%)	3 / 53 (5.66%)
occurrences (all)	0	0	7
Cardiac disorders			
Tachycardia			
subjects affected / exposed	3 / 178 (1.69%)	6 / 179 (3.35%)	0 / 53 (0.00%)
occurrences (all)	4	6	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	19 / 178 (10.67%)	16 / 179 (8.94%)	3 / 53 (5.66%)
occurrences (all)	23	21	4
Dysgeusia			
subjects affected / exposed	3 / 178 (1.69%)	2 / 179 (1.12%)	0 / 53 (0.00%)
occurrences (all)	3	2	0
Headache			
subjects affected / exposed	20 / 178 (11.24%)	29 / 179 (16.20%)	8 / 53 (15.09%)
occurrences (all)	31	40	11
Neuropathy peripheral			
subjects affected / exposed	3 / 178 (1.69%)	3 / 179 (1.68%)	0 / 53 (0.00%)
occurrences (all)	3	3	0
Paraesthesia			
subjects affected / exposed	4 / 178 (2.25%)	3 / 179 (1.68%)	0 / 53 (0.00%)
occurrences (all)	4	3	0
Tremor			
subjects affected / exposed	3 / 178 (1.69%)	5 / 179 (2.79%)	0 / 53 (0.00%)
occurrences (all)	3	5	0
Peripheral sensory neuropathy			
subjects affected / exposed	1 / 178 (0.56%)	2 / 179 (1.12%)	0 / 53 (0.00%)
occurrences (all)	1	2	0
Blood and lymphatic system disorders			

Anaemia			
subjects affected / exposed	29 / 178 (16.29%)	25 / 179 (13.97%)	12 / 53 (22.64%)
occurrences (all)	39	29	13
Leukopenia			
subjects affected / exposed	0 / 178 (0.00%)	3 / 179 (1.68%)	0 / 53 (0.00%)
occurrences (all)	0	4	0
Neutropenia			
subjects affected / exposed	1 / 178 (0.56%)	2 / 179 (1.12%)	0 / 53 (0.00%)
occurrences (all)	1	2	0
Thrombocytopenia			
subjects affected / exposed	3 / 178 (1.69%)	3 / 179 (1.68%)	0 / 53 (0.00%)
occurrences (all)	5	5	0
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	4 / 178 (2.25%)	9 / 179 (5.03%)	0 / 53 (0.00%)
occurrences (all)	8	10	0
Eye disorders			
Dry eye			
subjects affected / exposed	0 / 178 (0.00%)	0 / 179 (0.00%)	3 / 53 (5.66%)
occurrences (all)	0	0	3
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	11 / 178 (6.18%)	9 / 179 (5.03%)	0 / 53 (0.00%)
occurrences (all)	13	10	0
Abdominal pain			
subjects affected / exposed	28 / 178 (15.73%)	26 / 179 (14.53%)	7 / 53 (13.21%)
occurrences (all)	37	31	7
Abdominal pain upper			
subjects affected / exposed	6 / 178 (3.37%)	10 / 179 (5.59%)	0 / 53 (0.00%)
occurrences (all)	6	10	0
Constipation			
subjects affected / exposed	39 / 178 (21.91%)	42 / 179 (23.46%)	12 / 53 (22.64%)
occurrences (all)	46	54	14
Diarrhoea			
subjects affected / exposed	39 / 178 (21.91%)	36 / 179 (20.11%)	14 / 53 (26.42%)
occurrences (all)	51	62	19
Dry mouth			

subjects affected / exposed	9 / 178 (5.06%)	7 / 179 (3.91%)	0 / 53 (0.00%)
occurrences (all)	11	8	0
Dyspepsia			
subjects affected / exposed	3 / 178 (1.69%)	4 / 179 (2.23%)	4 / 53 (7.55%)
occurrences (all)	3	4	4
Nausea			
subjects affected / exposed	43 / 178 (24.16%)	49 / 179 (27.37%)	12 / 53 (22.64%)
occurrences (all)	70	55	12
Vomiting			
subjects affected / exposed	17 / 178 (9.55%)	38 / 179 (21.23%)	6 / 53 (11.32%)
occurrences (all)	24	58	7
Dysphagia			
subjects affected / exposed	0 / 178 (0.00%)	0 / 179 (0.00%)	3 / 53 (5.66%)
occurrences (all)	0	0	3
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	7 / 178 (3.93%)	2 / 179 (1.12%)	0 / 53 (0.00%)
occurrences (all)	8	4	0
Dry skin			
subjects affected / exposed	18 / 178 (10.11%)	17 / 179 (9.50%)	0 / 53 (0.00%)
occurrences (all)	23	17	0
Night sweats			
subjects affected / exposed	4 / 178 (2.25%)	9 / 179 (5.03%)	1 / 53 (1.89%)
occurrences (all)	4	10	1
Erythema			
subjects affected / exposed	10 / 178 (5.62%)	7 / 179 (3.91%)	0 / 53 (0.00%)
occurrences (all)	12	8	0
Pruritus			
subjects affected / exposed	49 / 178 (27.53%)	57 / 179 (31.84%)	6 / 53 (11.32%)
occurrences (all)	75	71	7
Rash			
subjects affected / exposed	29 / 178 (16.29%)	33 / 179 (18.44%)	11 / 53 (20.75%)
occurrences (all)	38	49	13
Rash maculo-papular			
subjects affected / exposed	10 / 178 (5.62%)	17 / 179 (9.50%)	3 / 53 (5.66%)
occurrences (all)	11	21	4

Vitiligo			
subjects affected / exposed	14 / 178 (7.87%)	15 / 179 (8.38%)	0 / 53 (0.00%)
occurrences (all)	18	18	0
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	16 / 178 (8.99%)	15 / 179 (8.38%)	4 / 53 (7.55%)
occurrences (all)	16	16	4
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	34 / 178 (19.10%)	23 / 179 (12.85%)	9 / 53 (16.98%)
occurrences (all)	47	33	12
Back pain			
subjects affected / exposed	23 / 178 (12.92%)	20 / 179 (11.17%)	3 / 53 (5.66%)
occurrences (all)	30	26	3
Bone pain			
subjects affected / exposed	2 / 178 (1.12%)	8 / 179 (4.47%)	0 / 53 (0.00%)
occurrences (all)	2	8	0
Muscular weakness			
subjects affected / exposed	5 / 178 (2.81%)	8 / 179 (4.47%)	0 / 53 (0.00%)
occurrences (all)	5	9	0
Myalgia			
subjects affected / exposed	18 / 178 (10.11%)	13 / 179 (7.26%)	3 / 53 (5.66%)
occurrences (all)	22	14	3
Musculoskeletal pain			
subjects affected / exposed	16 / 178 (8.99%)	14 / 179 (7.82%)	4 / 53 (7.55%)
occurrences (all)	18	14	5
Pain in extremity			
subjects affected / exposed	18 / 178 (10.11%)	17 / 179 (9.50%)	3 / 53 (5.66%)
occurrences (all)	22	22	3
Muscle spasms			
subjects affected / exposed	0 / 178 (0.00%)	0 / 179 (0.00%)	1 / 53 (1.89%)
occurrences (all)	0	0	1
Neck pain			
subjects affected / exposed	0 / 178 (0.00%)	0 / 179 (0.00%)	5 / 53 (9.43%)
occurrences (all)	0	0	5
Infections and infestations			

Nasopharyngitis			
subjects affected / exposed	10 / 178 (5.62%)	17 / 179 (9.50%)	3 / 53 (5.66%)
occurrences (all)	11	25	4
Upper respiratory tract infection			
subjects affected / exposed	7 / 178 (3.93%)	17 / 179 (9.50%)	4 / 53 (7.55%)
occurrences (all)	10	20	4
Urinary tract infection			
subjects affected / exposed	16 / 178 (8.99%)	17 / 179 (9.50%)	7 / 53 (13.21%)
occurrences (all)	18	22	7
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	35 / 178 (19.66%)	50 / 179 (27.93%)	9 / 53 (16.98%)
occurrences (all)	42	54	9
Dehydration			
subjects affected / exposed	7 / 178 (3.93%)	6 / 179 (3.35%)	0 / 53 (0.00%)
occurrences (all)	15	7	0
Hyperglycaemia			
subjects affected / exposed	12 / 178 (6.74%)	11 / 179 (6.15%)	0 / 53 (0.00%)
occurrences (all)	20	19	0
Hypertriglyceridaemia			
subjects affected / exposed	7 / 178 (3.93%)	9 / 179 (5.03%)	0 / 53 (0.00%)
occurrences (all)	15	22	0
Hypoalbuminaemia			
subjects affected / exposed	5 / 178 (2.81%)	11 / 179 (6.15%)	0 / 53 (0.00%)
occurrences (all)	6	12	0
Hypokalaemia			
subjects affected / exposed	9 / 178 (5.06%)	7 / 179 (3.91%)	4 / 53 (7.55%)
occurrences (all)	9	9	7
Hyponatraemia			
subjects affected / exposed	19 / 178 (10.67%)	10 / 179 (5.59%)	6 / 53 (11.32%)
occurrences (all)	28	11	9
Hyperkalaemia			
subjects affected / exposed	0 / 178 (0.00%)	0 / 179 (0.00%)	4 / 53 (7.55%)
occurrences (all)	0	0	4

Non-serious adverse events	ICC (After Switch to Pembrolizumab 10 mg/kg)		

Total subjects affected by non-serious adverse events subjects affected / exposed	36 / 45 (80.00%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps) Tumour pain subjects affected / exposed occurrences (all) Melanocytic naevus subjects affected / exposed occurrences (all)	 0 / 45 (0.00%) 0 0 / 45 (0.00%) 0		
Vascular disorders Hypotension subjects affected / exposed occurrences (all) Deep vein thrombosis subjects affected / exposed occurrences (all)	 3 / 45 (6.67%) 5 0 / 45 (0.00%) 0		
General disorders and administration site conditions Asthenia subjects affected / exposed occurrences (all) Chest pain subjects affected / exposed occurrences (all) Chills subjects affected / exposed occurrences (all) Fatigue subjects affected / exposed occurrences (all) Influenza like illness subjects affected / exposed occurrences (all) Malaise subjects affected / exposed occurrences (all) Oedema peripheral	 3 / 45 (6.67%) 3 0 / 45 (0.00%) 0 0 / 45 (0.00%) 0 15 / 45 (33.33%) 23 3 / 45 (6.67%) 6 0 / 45 (0.00%) 0		

subjects affected / exposed	2 / 45 (4.44%)		
occurrences (all)	2		
Pain			
subjects affected / exposed	0 / 45 (0.00%)		
occurrences (all)	0		
Pyrexia			
subjects affected / exposed	8 / 45 (17.78%)		
occurrences (all)	8		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	5 / 45 (11.11%)		
occurrences (all)	6		
Dyspnoea			
subjects affected / exposed	4 / 45 (8.89%)		
occurrences (all)	4		
Pleural effusion			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Depression			
subjects affected / exposed	0 / 45 (0.00%)		
occurrences (all)	0		
Insomnia			
subjects affected / exposed	0 / 45 (0.00%)		
occurrences (all)	0		
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	2 / 45 (4.44%)		
occurrences (all)	4		
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
Blood alkaline phosphatase increased			

subjects affected / exposed	2 / 45 (4.44%)		
occurrences (all)	2		
Blood bilirubin increased			
subjects affected / exposed	0 / 45 (0.00%)		
occurrences (all)	0		
Blood cholesterol increased			
subjects affected / exposed	0 / 45 (0.00%)		
occurrences (all)	0		
Lymphocyte count decreased			
subjects affected / exposed	0 / 45 (0.00%)		
occurrences (all)	0		
Neutrophil count decreased			
subjects affected / exposed	0 / 45 (0.00%)		
occurrences (all)	0		
Platelet count decreased			
subjects affected / exposed	0 / 45 (0.00%)		
occurrences (all)	0		
Weight decreased			
subjects affected / exposed	1 / 45 (2.22%)		
occurrences (all)	1		
White blood cell count decreased			
subjects affected / exposed	0 / 45 (0.00%)		
occurrences (all)	0		
Blood creatinine increased			
subjects affected / exposed	2 / 45 (4.44%)		
occurrences (all)	2		
Cardiac disorders			
Tachycardia			
subjects affected / exposed	0 / 45 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Dizziness			
subjects affected / exposed	7 / 45 (15.56%)		
occurrences (all)	7		
Dysgeusia			

subjects affected / exposed occurrences (all)	0 / 45 (0.00%) 0		
Headache subjects affected / exposed occurrences (all)	6 / 45 (13.33%) 10		
Neuropathy peripheral subjects affected / exposed occurrences (all)	0 / 45 (0.00%) 0		
Paraesthesia subjects affected / exposed occurrences (all)	0 / 45 (0.00%) 0		
Tremor subjects affected / exposed occurrences (all)	0 / 45 (0.00%) 0		
Peripheral sensory neuropathy subjects affected / exposed occurrences (all)	0 / 45 (0.00%) 0		
Blood and lymphatic system disorders			
Anaemia subjects affected / exposed occurrences (all)	8 / 45 (17.78%) 21		
Leukopenia subjects affected / exposed occurrences (all)	0 / 45 (0.00%) 0		
Neutropenia subjects affected / exposed occurrences (all)	0 / 45 (0.00%) 0		
Thrombocytopenia subjects affected / exposed occurrences (all)	0 / 45 (0.00%) 0		
Ear and labyrinth disorders			
Vertigo subjects affected / exposed occurrences (all)	0 / 45 (0.00%) 0		
Eye disorders			

Dry eye subjects affected / exposed occurrences (all)	0 / 45 (0.00%) 0		
Gastrointestinal disorders Abdominal distension subjects affected / exposed occurrences (all)	0 / 45 (0.00%) 0		
Abdominal pain subjects affected / exposed occurrences (all)	2 / 45 (4.44%) 3		
Abdominal pain upper subjects affected / exposed occurrences (all)	0 / 45 (0.00%) 0		
Constipation subjects affected / exposed occurrences (all)	5 / 45 (11.11%) 5		
Diarrhoea subjects affected / exposed occurrences (all)	9 / 45 (20.00%) 22		
Dry mouth subjects affected / exposed occurrences (all)	0 / 45 (0.00%) 0		
Dyspepsia subjects affected / exposed occurrences (all)	2 / 45 (4.44%) 2		
Nausea subjects affected / exposed occurrences (all)	10 / 45 (22.22%) 17		
Vomiting subjects affected / exposed occurrences (all)	2 / 45 (4.44%) 2		
Dysphagia subjects affected / exposed occurrences (all)	0 / 45 (0.00%) 0		
Skin and subcutaneous tissue disorders			

Alopecia subjects affected / exposed occurrences (all)	0 / 45 (0.00%) 0		
Dry skin subjects affected / exposed occurrences (all)	0 / 45 (0.00%) 0		
Night sweats subjects affected / exposed occurrences (all)	4 / 45 (8.89%) 4		
Erythema subjects affected / exposed occurrences (all)	0 / 45 (0.00%) 0		
Pruritus subjects affected / exposed occurrences (all)	5 / 45 (11.11%) 5		
Rash subjects affected / exposed occurrences (all)	7 / 45 (15.56%) 9		
Rash maculo-papular subjects affected / exposed occurrences (all)	1 / 45 (2.22%) 1		
Vitiligo subjects affected / exposed occurrences (all)	0 / 45 (0.00%) 0		
Endocrine disorders Hypothyroidism subjects affected / exposed occurrences (all)	3 / 45 (6.67%) 3		
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all)	8 / 45 (17.78%) 9		
Back pain subjects affected / exposed occurrences (all)	2 / 45 (4.44%) 2		
Bone pain			

subjects affected / exposed occurrences (all)	0 / 45 (0.00%) 0		
Muscular weakness subjects affected / exposed occurrences (all)	0 / 45 (0.00%) 0		
Myalgia subjects affected / exposed occurrences (all)	3 / 45 (6.67%) 3		
Musculoskeletal pain subjects affected / exposed occurrences (all)	2 / 45 (4.44%) 2		
Pain in extremity subjects affected / exposed occurrences (all)	1 / 45 (2.22%) 4		
Muscle spasms subjects affected / exposed occurrences (all)	3 / 45 (6.67%) 6		
Neck pain subjects affected / exposed occurrences (all)	1 / 45 (2.22%) 1		
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all)	0 / 45 (0.00%) 0		
Upper respiratory tract infection subjects affected / exposed occurrences (all)	3 / 45 (6.67%) 3		
Urinary tract infection subjects affected / exposed occurrences (all)	2 / 45 (4.44%) 2		
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	8 / 45 (17.78%) 8		
Dehydration			

subjects affected / exposed	0 / 45 (0.00%)		
occurrences (all)	0		
Hyperglycaemia			
subjects affected / exposed	0 / 45 (0.00%)		
occurrences (all)	0		
Hypertriglyceridaemia			
subjects affected / exposed	0 / 45 (0.00%)		
occurrences (all)	0		
Hypoalbuminaemia			
subjects affected / exposed	0 / 45 (0.00%)		
occurrences (all)	0		
Hypokalaemia			
subjects affected / exposed	3 / 45 (6.67%)		
occurrences (all)	3		
Hyponatraemia			
subjects affected / exposed	3 / 45 (6.67%)		
occurrences (all)	4		
Hyperkalaemia			
subjects affected / exposed	0 / 45 (0.00%)		
occurrences (all)	0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
25 April 2013	Amendment 01: The primary reasons for the amendment were to: 1) modify the primary and secondary objectives; 2) clarify inclusion and exclusion criteria; 3) modify the standard of care chemotherapy comparators permitted in this trial; and 4) modify the statistical analysis plan.
02 October 2013	Amendment 02: The primary reasons for the amendment were to: 1) modify the primary and secondary objectives; 2) clarify inclusion and exclusion criteria; 3) modify the standard of care chemotherapy comparators permitted in this trial; and 4) modify the statistical analysis plan.
14 July 2016	Amendment 03: The primary reason for the amendment was to modify the dosage of study treatment so that all participants will receive a fixed dose of pembrolizumab 200 mg every 3 weeks.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported