Clinical trial results:
A Randomized Open-Label Phase III Trial of Pembrolizumab versus Platinum based Chemotherapy in 1L Subjects with PD-L1 Strong Metastatic Non-Small Cell Lung Cancer

Summary

EudraCT number	2014-000323-25
Trial protocol	IT IE HU DE ES BE NL FR AT
Global end of trial date	27 May 2021

Results information

Result version number	v1 (current)
This version publication date	03 June 2022
First version publication date	03 June 2022

Trial information

Trial identification

Sponsor protocol code	3475-024

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02142738
WHO universal trial number (UTN)	-
Other trial identifiers	JAPIC: 142728

Notes:

Sponsors

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

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	27 May 2021
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	27 May 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This is a study to assess the efficacy and safety of pembrolizumab (MK-3475/SCH 900475) compared to standard of care (SOC) platinum-based chemotherapies in the treatment of participants with previously untreated stage IV, programmed cell death ligand 1 (PD-L1) strong expressing Non-Small Cell Lung Cancer (NSCLC). The primary hypothesis of this study is that participants with PD-L1 strong NSCLC will have a longer Progression Free Survival (PFS), as assessed by Response Evaluation Criteria in Solid Tumors version 1.1 (RECIST 1.1) when treated with pembrolizumab than when treated with SOC platinum-based chemotherapies.

With Amendment 09 (20 December 2017), once participants have achieved the study objective or the study has ended, participants will be discontinued from this study and enrolled in an extension study to continue protocol-defined assessments and treatment.

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	25 August 2014
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 21
Country: Number of subjects enrolled	Austria: 4
Country: Number of subjects enrolled	Belgium: 5
Country: Number of subjects enrolled	Canada: 15
Country: Number of subjects enrolled	France: 11
Country: Number of subjects enrolled	Germany: 23
Country: Number of subjects enrolled	Hungary: 28
Country: Number of subjects enrolled	Ireland: 8
Country: Number of subjects enrolled	Israel: 28
Country: Number of subjects enrolled	Italy: 21
Country: Number of subjects enrolled	Japan: 40
Country: Number of subjects enrolled	Netherlands: 4
Country: Number of subjects enrolled	New Zealand: 2
Country: Number of subjects enrolled	Spain: 33

Country: Number of subjects enrolled	United Kingdom: 21
Country: Number of subjects enrolled	United States: 41
Worldwide total number of subjects	305
EEA total number of subjects	137

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	141
From 65 to 84 years	159
85 years and over	5

Subject disposition

Recruitment

Recruitment details:

Participants with Non-Small Cell Lung Cancer (NSCLC) were enrolled in this study.

Pre-assignment

Screening details:

Per protocol, it was planned that participants would be randomized 1:1 to receive either pembrolizumab or investigator-choice standard of care (SOC) chemotherapy and data analysis would be conducted on the two treatment arms: Pembrolizumab and SOC Chemotherapy.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Pembrolizumab

Arm description:

Participants received pembrolizumab 200 mg, administered as intravenous (IV) infusion on Day 1 of each 21-day cycle for up to 35 cycles or until documented progressive disease (PD) or participant discontinuation.

Arm type	Experimental
Investigational medicinal product name	Pembrolizumab
Investigational medicinal product code	
Other name	KEYTRUDA® MK-3475 SCH 900475
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

200 mg Every 3 Weeks (Q3W)

Arm title	SOC Chemotherapy

Arm description:

Participants received 1 of 5 possible standard chemotherapy regimens at the investigator's discretion by IV infusion administered on 21-day cycles for 4-6 cycles or until progressive disease or participant discontinuation: paclitaxel 200 mg/m^2 and carboplatin Area Under the Curve (AUC) 5 or 6 on Day 1 of each cycle; pemetrexed 500 mg/m^2 and carboplatin AUC 5 or 6 on Day 1 of each cycle; pemetrexed 500 mg/m^2 and cisplatin 75 mg/m^2 on Day 1 of each cycle; gemcitabine 1250 mg/m^2 on Days 1 and 8 of each cycle and carboplatin AUC 5 or 6 on Day 1 of a cycle or gemcitabine 1250 mg/m^2 on Days 1 and 8 of each cycle and cisplatin 75 mg/m^2 on Day 1 of each cycle. Participants with PD following chemotherapy can switch to pembrolizumab for up to 35 cycles. Participants who switched to and then stopped pembrolizumab and had stable disease but progressed after discontinuation, initiate a second course of pembrolizumab at the investigator’s discretion for up to 17 cycles.

Arm type	Active comparator
Investigational medicinal product name	Paclitaxel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

200 mg/m^2 Q3W

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

Dosage and administration details:
Area Under the Curve (AUC) 5 or 6 Q3W

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

Dosage and administration details:
75 mg/m^2 Q3W

Investigational medicinal product name	Pemetrexed
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for infusion
Routes of administration	Intravenous use

Dosage and administration details:
500 mg/m^2 Q3W

Investigational medicinal product name	Gemcitabine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for infusion
Routes of administration	Intravascular use

Dosage and administration details:
1250 mg/m^2 on Days 1 and 8 of each 21-day cycle

Number of subjects in period 1	Pembrolizumab	SOC Chemotherapy
Started	154	151
Treated	154	150
Chemotherapy Switch to Pembrolizumab	0	83
Second Course Pembrolizumab	12	1
Completed	0	0
Not completed	154	151
Adverse event, serious fatal	92	112
Consent withdrawn by subject	6	7
Adverse event, non-fatal	13	9
Follow up ended by sponsor	43	20
Lost to follow-up	-	3

Baseline characteristics

Reporting groups	
Reporting group title	Pembrolizumab
Reporting group description:	
Participants received pembrolizumab 200 mg, administered as intravenous (IV) infusion on Day 1 of each 21-day cycle for up to 35 cycles or until documented progressive disease (PD) or participant discontinuation.	
Reporting group title	SOC Chemotherapy
Reporting group description:	
Participants received 1 of 5 possible standard chemotherapy regimens at the investigator's discretion by IV infusion administered on 21-day cycles for 4-6 cycles or until progressive disease or participant discontinuation: paclitaxel 200 mg/m^2 and carboplatin Area Under the Curve (AUC) 5 or 6 on Day 1 of each cycle; pemetrexed 500 mg/m^2 and carboplatin AUC 5 or 6 on Day 1 of each cycle; pemetrexed 500 mg/m^2 and cisplatin 75 mg/m^2 on Day 1 of each cycle; gemcitabine 1250 mg/m^2 on Days 1 and 8 of each cycle and carboplatin AUC 5 or 6 on Day 1 of a cycle or gemcitabine 1250 mg/m^2 on Days 1 and 8 of each cycle and cisplatin 75 mg/m^2 on Day 1 of each cycle. Participants with PD following chemotherapy can switch to pembrolizumab for up to 35 cycles. Participants who switched to and then stopped pembrolizumab and had stable disease but progressed after discontinuation, initiate a second course of pembrolizumab at the investigator’s discretion for up to 17 cycles.	

Reporting group values	Pembrolizumab	SOC Chemotherapy	Total
Number of subjects	154	151	305
Age categorical Units: Participants			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	77	64	141
From 65-84 years	74	85	159
85 years and over	3	2	5
Age Continuous Units: Years			
arithmetic mean	63.9	64.6	
standard deviation	± 10.1	± 9.5	-
Sex: Female, Male Units: Participants			
Female	62	56	118
Male	92	95	187
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	1	1
Asian	25	21	46
Native Hawaiian or Other Pacific Islander	0	1	1
Black or African American	2	2	4
White	125	126	251
More than one race	0	0	0

Unknown or Not Reported	2	0	2
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	1	5	6
Not Hispanic or Latino	148	135	283
Unknown or Not Reported	5	11	16
Eastern Cooperative Oncology Group (ECOG) Status (0, 1 or 2)			
Eastern Cooperative Oncology Group (ECOG) Performance. ECOG is presented where 0 = Fully active, no performance restrictions; 1 = Strenuous physical activity restricted, fully ambulatory & able to carry out light work; and 2 = In bed <50% of the time, ambulatory and capable of all self-care, but unable to carry out any work activities			
Units: Subjects			
ECOG = 0	54	53	107
ECOG = 1	99	98	197
ECOG = 2	1	0	1
Histology			
Participants were categorized according to the histology of their carcinoma			
Units: Subjects			
ADENOCARCINOMA	104	108	212
ADENOSQUAMOUS	2	2	4
LARGE CELL CARCINOMA	2	2	4
NON-SQUAMOUS CELL CARCINOMA	5	7	12
POORLY DIFFERENTIATED	9	3	12
SARCOMATOID	3	2	5
SQUAMOUS CELL CARCINOMA	29	26	55
POORLY DIFFERENTIATED SQUAMOUS CELL CARCINOMA	0	1	1
Geographic Region of Enrolling Site Units: Subjects			
Non-East Asia	133	132	265
East Asia	21	19	40

End points

End points reporting groups

Reporting group title	Pembrolizumab

Reporting group description:

Participants received pembrolizumab 200 mg, administered as intravenous (IV) infusion on Day 1 of each 21-day cycle for up to 35 cycles or until documented progressive disease (PD) or participant discontinuation.

Reporting group title	SOC Chemotherapy

Reporting group description:

Participants received 1 of 5 possible standard chemotherapy regimens at the investigator's discretion by IV infusion administered on 21-day cycles for 4-6 cycles or until progressive disease or participant discontinuation: paclitaxel 200 mg/m^2 and carboplatin Area Under the Curve (AUC) 5 or 6 on Day 1 of each cycle; pemetrexed 500 mg/m^2 and carboplatin AUC 5 or 6 on Day 1 of each cycle; pemetrexed 500 mg/m^2 and cisplatin 75 mg/m^2 on Day 1 of each cycle; gemcitabine 1250 mg/m^2 on Days 1 and 8 of each cycle and carboplatin AUC 5 or 6 on Day 1 of a cycle or gemcitabine 1250 mg/m^2 on Days 1 and 8 of each cycle and cisplatin 75 mg/m^2 on Day 1 of each cycle. Participants with PD following chemotherapy can switch to pembrolizumab for up to 35 cycles. Participants who switched to and then stopped pembrolizumab and had stable disease but progressed after discontinuation, initiate a second course of pembrolizumab at the investigator’s discretion for up to 17 cycles.

Primary: Progression Free Survival (PFS) Rate at Month 6

End point title	Progression Free Survival (PFS) Rate at Month 6

End point description:

PFS was defined as the time from randomization to documented disease progression per RECIST 1.1 or death due to any cause, whichever occurred first and was based on blinded independent central radiologists’ (BICR) review. Progressive Disease (PD) was defined as ≥20% increase in the sum of diameters of target lesions and an absolute increase of ≥5 mm. (Note: the appearance of one or more new lesions was also considered progression). Participants were evaluated every 9 weeks with radiographic imaging to assess their response to treatment. The data cutoff date was 09-May-2016. The PFS rate at Month 6 was calculated. The Intention-to-treat (ITT) population included all randomized participants. Participants were included in the treatment group to which they were randomized, regardless of whether or not they received study treatment.

End point type	Primary

End point timeframe:

Month 6

End point values	Pembrolizumab	SOC Chemotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	154	151		
Units: Percentage of Participants				
number (confidence interval 95%)	62.1 (53.8 to 69.4)	50.3 (41.9 to 58.2)		

Statistical analyses

Statistical analysis title	Superiority of Pembrolizumab versus SOC

Statistical analysis description:

Treatment as a covariate stratified by geographic region (East Asia vs. non-East Asia), ECOG PS (0 vs. 1) and histology (squamous vs. nonsquamous).

Comparison groups	Pembrolizumab v SOC Chemotherapy
Number of subjects included in analysis	305
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [1]
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.37
upper limit	0.68

Notes:

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

Secondary: Overall Survival (OS) Rate

End point title	Overall Survival (OS) Rate

End point description:

OS was defined as the time from randomization to death due to any cause. Participants without documented death at the time of the analysis were censored at the date of the last follow-up. The data cutoff date was 10-July-2017. The median OS rate is presented for month 12. The ITT population included all randomized participants. Participants were included in the treatment group to which they were randomized, regardless of whether or not they received study treatment.

End point type	Secondary

End point timeframe:

12 months

End point values	Pembrolizumab	SOC Chemotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	154	151		
Units: Percentage of Participants				
number (confidence interval 95%)	70.3 (62.3 to 76.9)	54.8 (46.4 to 62.4)		

Statistical analyses

Statistical analysis title	Superiority of Pembrolizumab to SOC

Statistical analysis description:

Treatment as a covariate stratified by geographic region (East Asia vs. non-East Asia), ECOG PS (0 vs. 1) and histology (squamous vs. nonsquamous).

Comparison groups	Pembrolizumab v SOC Chemotherapy

Number of subjects included in analysis	305
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.002 [2]
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.63
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.47
upper limit	0.86

Notes:

[2] - One-sided p-value based on log-rank test

Secondary: Objective Response Rate (ORR)

End point title	Objective Response Rate (ORR)

End point description:

ORR was defined as the percentage of participants in the analysis population who experienced a Complete Response (CR; disappearance of all target lesions) or a Partial Response (PR; at least a 30% decrease in the sum of diameters of target lesions) and was assessed using RECIST 1.1 based on BICR evaluation. ORR was assessed from enrollment/treatment initiation of a participant through data cutoff date of 09-May-2016. The Intention-to-treat (ITT) population included all randomized participants. Participants were included in the treatment group to which they were randomized, regardless of whether or not they received study treatment.

End point type	Secondary

End point timeframe:

Up to approximately 1.6 years

End point values	Pembrolizumab	SOC Chemotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	154	151		
Units: Percentage of Participants				
number (confidence interval 95%)	44.8 (36.8 to 53.0)	27.8 (20.8 to 35.7)		

Statistical analyses

Statistical analysis title	Superiority of Pembrolizumab versus SOC

Statistical analysis description:

Treatment as a covariate stratified by geographic region (East Asia vs. non-East Asia), ECOG PS (0 vs. 1) and histology (squamous vs. nonsquamous).

Comparison groups	Pembrolizumab v SOC Chemotherapy

Number of subjects included in analysis	305
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0011 [3]
Method	Miettinen & Nurminen method
Parameter estimate	Difference in percentages
Point estimate	16.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	6
upper limit	27

Notes:

[3] - One-sided p-value for testing

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to approximately 80 months.

Adverse event reporting additional description:

Deaths: All randomized participants (the number at risk for SOC Chemotherapy first course is 151). Safety: All randomized participants who got ≥1 dose of study drug. Per protocol MedDRA preferred terms "Neoplasm progression" and "Malignant neoplasm progression" not related to study drug are excluded as AEs.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.1

Reporting groups

Reporting group title	Pembrolizumab First Course

Reporting group description:

Participants received pembrolizumab 200 mg, administered as intravenous (IV) infusion on Day 1 of each 21-day cycle for up to 35 cycles or until documented progressive disease (PD) or participant discontinuation.

Reporting group title	SOC Chemotherapy First Course

Reporting group description:

Participants received 1 of 5 possible standard chemotherapy regimens at the investigator's discretion by IV infusion administered on 21-day cycles for 4-6 cycles or until progressive disease or participant discontinuation: paclitaxel 200 mg/m^2 and carboplatin Area Under the Curve (AUC) 5 or 6 on Day 1 of each cycle; pemetrexed 500 mg/m^2 and carboplatin AUC 5 or 6 on Day 1 of each cycle; pemetrexed 500 mg/m^2 and cisplatin 75 mg/m^2 on Day 1 of each cycle; gemcitabine 1250 mg/m^2 on Days 1 and 8 of each cycle and carboplatin AUC 5 or 6 on Day 1 of a cycle or gemcitabine 1250 mg/m^2 on Days 1 and 8 of each cycle and cisplatin 75 mg/m^2 on Day 1 of each cycle. Participants with PD following chemotherapy can switch to pembrolizumab for up to 35 cycles. Participants who switched to and then stopped pembrolizumab and had stable disease but progressed after discontinuation, initiate a second course of pembrolizumab at the investigator’s discretion for up to 17 cycles.

Reporting group title	SOC Chemotherapy Switched over to Second Course Pembrolizumab

Reporting group description:

One qualified participant received SOC chemotherapy first course, but continued to experience disease progression and at investigator's discretion switched to a course of pembrolizumab IV 200 mg, every cycle (three weeks) for up to 35 cycles up to ~2 years. The participant then initiated a second course of pembrolizumab at the same dose and schedule for up to ~1 additional year until documented PD or participant discontinuation.

Reporting group title	Pembrolizumab Second Course

Reporting group description:

Qualified participants who received the pembrolizumab first course and achieved CR, PR, or stable disease, and progressed after discontinuation, at the investigator's discretion, initiated a second course of pembrolizumab at the same dose and schedule for up to 17 cycles (approximately 1 additional year).

Reporting group title	SOC Chemotherapy Switched Over to Pembrolizumab First Course

Reporting group description:

Qualified participants who received the SOC chemotherapy first course but continued to experience disease progression, at the investigator's discretion, initiated a course of pembrolizumab IV 200 mg, every cycle (three weeks) for up to 35 cycles up to ~2 years.

Serious adverse events	Pembrolizumab First Course	SOC Chemotherapy First Course	SOC Chemotherapy Switched over to Second Course Pembrolizumab
Total subjects affected by serious adverse events			
subjects affected / exposed	79 / 154 (51.30%)	70 / 150 (46.67%)	0 / 1 (0.00%)
number of deaths (all causes)	103	60	1
number of deaths resulting from adverse events	2	3	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Bladder neoplasm			
subjects affected / exposed	0 / 154 (0.00%)	1 / 150 (0.67%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cancer pain			
subjects affected / exposed	0 / 154 (0.00%)	1 / 150 (0.67%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infected neoplasm			
subjects affected / exposed	1 / 154 (0.65%)	0 / 150 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malignant neoplasm progression			
subjects affected / exposed	0 / 154 (0.00%)	1 / 150 (0.67%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendix cancer			
subjects affected / exposed	1 / 154 (0.65%)	0 / 150 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bladder cancer			
subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bladder transitional cell carcinoma			

subjects affected / exposed	1 / 154 (0.65%)	0 / 150 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colon cancer			
subjects affected / exposed	1 / 154 (0.65%)	0 / 150 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colorectal adenocarcinoma			
subjects affected / exposed	1 / 154 (0.65%)	0 / 150 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Vasospasm			
subjects affected / exposed	0 / 154 (0.00%)	1 / 150 (0.67%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Embolism			
subjects affected / exposed	0 / 154 (0.00%)	1 / 150 (0.67%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemia			
subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Superior vena cava occlusion			
subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	0 / 154 (0.00%)	1 / 150 (0.67%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Death			
subjects affected / exposed	0 / 154 (0.00%)	2 / 150 (1.33%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 2	0 / 0
Face oedema			
subjects affected / exposed	1 / 154 (0.65%)	0 / 150 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fatigue			
subjects affected / exposed	1 / 154 (0.65%)	1 / 150 (0.67%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gait disturbance			
subjects affected / exposed	0 / 154 (0.00%)	1 / 150 (0.67%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General physical health deterioration			
subjects affected / exposed	1 / 154 (0.65%)	0 / 150 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Multiple organ dysfunction syndrome			
subjects affected / exposed	1 / 154 (0.65%)	0 / 150 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Oedema peripheral			
subjects affected / exposed	1 / 154 (0.65%)	0 / 150 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	2 / 154 (1.30%)	1 / 150 (0.67%)	0 / 1 (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
Sudden death			

subjects affected / exposed	1 / 154 (0.65%)	0 / 150 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Immune system disorders			
Anaphylactic shock			
subjects affected / exposed	2 / 154 (1.30%)	0 / 150 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Hypersensitivity			
subjects affected / exposed	1 / 154 (0.65%)	0 / 150 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anaphylactic reaction			
subjects affected / exposed	1 / 154 (0.65%)	0 / 150 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Ovarian haemorrhage			
subjects affected / exposed	1 / 154 (0.65%)	0 / 150 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	1 / 154 (0.65%)	0 / 150 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Atelectasis			
subjects affected / exposed	1 / 154 (0.65%)	0 / 150 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchial obstruction			

subjects affected / exposed	0 / 154 (0.00%)	1 / 150 (0.67%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic obstructive pulmonary disease			
subjects affected / exposed	4 / 154 (2.60%)	1 / 150 (0.67%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 6	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epistaxis			
subjects affected / exposed	0 / 154 (0.00%)	2 / 150 (1.33%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemoptysis			
subjects affected / exposed	2 / 154 (1.30%)	0 / 150 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Painful respiration			
subjects affected / exposed	1 / 154 (0.65%)	0 / 150 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion			
subjects affected / exposed	6 / 154 (3.90%)	3 / 150 (2.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 6	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonitis			
subjects affected / exposed	6 / 154 (3.90%)	1 / 150 (0.67%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	6 / 6	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumothorax			
subjects affected / exposed	1 / 154 (0.65%)	1 / 150 (0.67%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary alveolar haemorrhage			

subjects affected / exposed	0 / 154 (0.00%)	1 / 150 (0.67%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Pulmonary embolism			
subjects affected / exposed	2 / 154 (1.30%)	2 / 150 (1.33%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Pulmonary oedema			
subjects affected / exposed	0 / 154 (0.00%)	2 / 150 (1.33%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure			
subjects affected / exposed	1 / 154 (0.65%)	0 / 150 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Acute respiratory distress syndrome			
subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune-mediated lung disease			
subjects affected / exposed	2 / 154 (1.30%)	0 / 150 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Laryngeal oedema			
subjects affected / exposed	1 / 154 (0.65%)	0 / 150 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 154 (0.00%)	1 / 150 (0.67%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Restlessness			

subjects affected / exposed	0 / 154 (0.00%)	1 / 150 (0.67%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Confusional state			
subjects affected / exposed	1 / 154 (0.65%)	0 / 150 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	2 / 154 (1.30%)	0 / 150 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	3 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 154 (0.65%)	0 / 150 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bilirubin conjugated increased			
subjects affected / exposed	1 / 154 (0.65%)	0 / 150 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Platelet count decreased			
subjects affected / exposed	0 / 154 (0.00%)	1 / 150 (0.67%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transaminases increased			
subjects affected / exposed	1 / 154 (0.65%)	0 / 150 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood corticotrophin decreased			
subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood creatinine increased			

subjects affected / exposed	1 / 154 (0.65%)	0 / 150 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cortisol decreased			
subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Infusion related reaction			
subjects affected / exposed	1 / 154 (0.65%)	0 / 150 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary radiation injury			
subjects affected / exposed	0 / 154 (0.00%)	1 / 150 (0.67%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Radiation oesophagitis			
subjects affected / exposed	0 / 154 (0.00%)	1 / 150 (0.67%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rib fracture			
subjects affected / exposed	0 / 154 (0.00%)	1 / 150 (0.67%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Toxicity to various agents			
subjects affected / exposed	0 / 154 (0.00%)	1 / 150 (0.67%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anastomotic complication			
subjects affected / exposed	1 / 154 (0.65%)	0 / 150 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			

Angina pectoris			
subjects affected / exposed	0 / 154 (0.00%)	1 / 150 (0.67%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial fibrillation			
subjects affected / exposed	1 / 154 (0.65%)	2 / 150 (1.33%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bradycardia			
subjects affected / exposed	0 / 154 (0.00%)	1 / 150 (0.67%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac arrest			
subjects affected / exposed	2 / 154 (1.30%)	1 / 150 (0.67%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 2	0 / 1	0 / 0
Cardiac failure			
subjects affected / exposed	1 / 154 (0.65%)	2 / 150 (1.33%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Cardio-respiratory arrest			
subjects affected / exposed	0 / 154 (0.00%)	1 / 150 (0.67%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Coronary artery disease			
subjects affected / exposed	1 / 154 (0.65%)	1 / 150 (0.67%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic cardiomyopathy			
subjects affected / exposed	0 / 154 (0.00%)	1 / 150 (0.67%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pericardial effusion			

subjects affected / exposed	1 / 154 (0.65%)	1 / 150 (0.67%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pericarditis			
subjects affected / exposed	1 / 154 (0.65%)	0 / 150 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Right ventricular failure			
subjects affected / exposed	0 / 154 (0.00%)	1 / 150 (0.67%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Supraventricular tachycardia			
subjects affected / exposed	1 / 154 (0.65%)	1 / 150 (0.67%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute myocardial infarction			
subjects affected / exposed	1 / 154 (0.65%)	0 / 150 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Cerebral infarction			
subjects affected / exposed	0 / 154 (0.00%)	1 / 150 (0.67%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrovascular accident			
subjects affected / exposed	1 / 154 (0.65%)	1 / 150 (0.67%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhagic stroke			
subjects affected / exposed	1 / 154 (0.65%)	0 / 150 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Ischaemic stroke			

subjects affected / exposed	1 / 154 (0.65%)	1 / 150 (0.67%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient ischaemic attack			
subjects affected / exposed	0 / 154 (0.00%)	1 / 150 (0.67%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Brain injury			
subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Brown-Sequard syndrome			
subjects affected / exposed	1 / 154 (0.65%)	0 / 150 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral haemorrhage			
subjects affected / exposed	0 / 154 (0.00%)	1 / 150 (0.67%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Encephalopathy			
subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 154 (1.30%)	5 / 150 (3.33%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 3	5 / 6	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile neutropenia			
subjects affected / exposed	0 / 154 (0.00%)	3 / 150 (2.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	3 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Leukocytosis			

subjects affected / exposed	0 / 154 (0.00%)	1 / 150 (0.67%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancytopenia			
subjects affected / exposed	0 / 154 (0.00%)	3 / 150 (2.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	3 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopenia			
subjects affected / exposed	0 / 154 (0.00%)	3 / 150 (2.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	3 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombotic microangiopathy			
subjects affected / exposed	0 / 154 (0.00%)	1 / 150 (0.67%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 154 (0.65%)	0 / 150 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis			
subjects affected / exposed	2 / 154 (1.30%)	0 / 150 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Constipation			
subjects affected / exposed	0 / 154 (0.00%)	1 / 150 (0.67%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			

subjects affected / exposed	3 / 154 (1.95%)	1 / 150 (0.67%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	4 / 4	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enterocolitis			
subjects affected / exposed	1 / 154 (0.65%)	0 / 150 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Faecaloma			
subjects affected / exposed	0 / 154 (0.00%)	1 / 150 (0.67%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric ulcer			
subjects affected / exposed	1 / 154 (0.65%)	0 / 150 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastritis erosive			
subjects affected / exposed	2 / 154 (1.30%)	0 / 150 (0.00%)	0 / 1 (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
Nausea			
subjects affected / exposed	0 / 154 (0.00%)	2 / 150 (1.33%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis			
subjects affected / exposed	1 / 154 (0.65%)	0 / 150 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal obstruction			
subjects affected / exposed	0 / 154 (0.00%)	1 / 150 (0.67%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stomatitis			

subjects affected / exposed	0 / 154 (0.00%)	1 / 150 (0.67%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	1 / 154 (0.65%)	0 / 150 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastritis			
subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal obstruction			
subjects affected / exposed	1 / 154 (0.65%)	0 / 150 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophagitis			
subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oral lichen planus			
subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Acute hepatic failure			
subjects affected / exposed	1 / 154 (0.65%)	0 / 150 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Autoimmune hepatitis			
subjects affected / exposed	1 / 154 (0.65%)	0 / 150 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			

Lichenoid keratosis			
subjects affected / exposed	1 / 154 (0.65%)	0 / 150 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rash			
subjects affected / exposed	1 / 154 (0.65%)	0 / 150 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lichen planus			
subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rash maculo-papular			
subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 154 (0.00%)	3 / 150 (2.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertensive nephropathy			
subjects affected / exposed	0 / 154 (0.00%)	1 / 150 (0.67%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tubulointerstitial nephritis			
subjects affected / exposed	1 / 154 (0.65%)	0 / 150 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
Hyperthyroidism			
subjects affected / exposed	1 / 154 (0.65%)	0 / 150 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Hypophysitis			
subjects affected / exposed	1 / 154 (0.65%)	0 / 150 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 154 (0.65%)	2 / 150 (1.33%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Back pain			
subjects affected / exposed	1 / 154 (0.65%)	3 / 150 (2.00%)	0 / 1 (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
Osteolysis			
subjects affected / exposed	1 / 154 (0.65%)	0 / 150 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal pain			
subjects affected / exposed	1 / 154 (0.65%)	0 / 150 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematoma muscle			
subjects affected / exposed	0 / 154 (0.00%)	1 / 150 (0.67%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Muscular weakness			
subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Appendicitis			
subjects affected / exposed	1 / 154 (0.65%)	0 / 150 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Bronchitis			
subjects affected / exposed	1 / 154 (0.65%)	0 / 150 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	1 / 154 (0.65%)	1 / 150 (0.67%)	0 / 1 (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
Clostridium difficile colitis			
subjects affected / exposed	1 / 154 (0.65%)	2 / 150 (1.33%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis viral			
subjects affected / exposed	1 / 154 (0.65%)	0 / 150 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infectious pleural effusion			
subjects affected / exposed	2 / 154 (1.30%)	0 / 150 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Infective exacerbation of chronic obstructive airways disease			
subjects affected / exposed	2 / 154 (1.30%)	1 / 150 (0.67%)	0 / 1 (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
Lower respiratory tract infection			
subjects affected / exposed	5 / 154 (3.25%)	3 / 150 (2.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	2 / 5	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenic sepsis			
subjects affected / exposed	1 / 154 (0.65%)	1 / 150 (0.67%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Oral candidiasis			

subjects affected / exposed	1 / 154 (0.65%)	0 / 150 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peritonsillar abscess			
subjects affected / exposed	0 / 154 (0.00%)	1 / 150 (0.67%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	6 / 154 (3.90%)	13 / 150 (8.67%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 7	5 / 13	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Pulmonary sepsis			
subjects affected / exposed	0 / 154 (0.00%)	2 / 150 (1.33%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Respiratory tract infection			
subjects affected / exposed	0 / 154 (0.00%)	2 / 150 (1.33%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	1 / 154 (0.65%)	1 / 150 (0.67%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic shock			
subjects affected / exposed	0 / 154 (0.00%)	1 / 150 (0.67%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin infection			
subjects affected / exposed	0 / 154 (0.00%)	1 / 150 (0.67%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Splenic abscess			

subjects affected / exposed	1 / 154 (0.65%)	0 / 150 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	1 / 154 (0.65%)	2 / 150 (1.33%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urosepsis			
subjects affected / exposed	2 / 154 (1.30%)	0 / 150 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bursitis infective			
subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Encephalomyelitis			
subjects affected / exposed	1 / 154 (0.65%)	0 / 150 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymph gland infection			
subjects affected / exposed	1 / 154 (0.65%)	0 / 150 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meningitis viral			
subjects affected / exposed	1 / 154 (0.65%)	0 / 150 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 154 (0.65%)	0 / 150 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dehydration			

subjects affected / exposed	1 / 154 (0.65%)	0 / 150 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetes mellitus			
subjects affected / exposed	1 / 154 (0.65%)	0 / 150 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetic ketoacidosis			
subjects affected / exposed	1 / 154 (0.65%)	0 / 150 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypercalcaemia			
subjects affected / exposed	0 / 154 (0.00%)	3 / 150 (2.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypocalcaemia			
subjects affected / exposed	0 / 154 (0.00%)	1 / 150 (0.67%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperglycaemia			
subjects affected / exposed	3 / 154 (1.95%)	0 / 150 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemia			
subjects affected / exposed	4 / 154 (2.60%)	0 / 150 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 5	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypovolaemia			
subjects affected / exposed	1 / 154 (0.65%)	0 / 150 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fluid overload			

subjects affected / exposed	1 / 154 (0.65%)	0 / 150 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypokalaemia			
subjects affected / exposed	1 / 154 (0.65%)	0 / 150 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Type 2 diabetes mellitus			
subjects affected / exposed	1 / 154 (0.65%)	0 / 150 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Pembrolizumab Second Course	SOC Chemotherapy Switched Over to Pembrolizumab First Course	
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 12 (16.67%)	27 / 83 (32.53%)	
number of deaths (all causes)	4	62	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Bladder neoplasm			
subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cancer pain			
subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infected neoplasm			
subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malignant neoplasm progression			

subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendix cancer			
subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder cancer			
subjects affected / exposed	0 / 12 (0.00%)	1 / 83 (1.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder transitional cell carcinoma			
subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colon cancer			
subjects affected / exposed	0 / 12 (0.00%)	1 / 83 (1.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colorectal adenocarcinoma			
subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Vasospasm			
subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Embolism			
subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemia			

subjects affected / exposed	0 / 12 (0.00%)	1 / 83 (1.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Superior vena cava occlusion			
subjects affected / exposed	1 / 12 (8.33%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Death			
subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Face oedema			
subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fatigue			
subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gait disturbance			
subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General physical health deterioration			
subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple organ dysfunction syndrome			

subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oedema peripheral			
subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sudden death			
subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Anaphylactic shock			
subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypersensitivity			
subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anaphylactic reaction			
subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Ovarian haemorrhage			
subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atelectasis			
subjects affected / exposed	0 / 12 (0.00%)	1 / 83 (1.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchial obstruction			
subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 12 (0.00%)	1 / 83 (1.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epistaxis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemoptysis			
subjects affected / exposed	0 / 12 (0.00%)	1 / 83 (1.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Painful respiration			
subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			
subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Pneumonitis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumothorax			
subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary alveolar haemorrhage			
subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary oedema			
subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute respiratory distress syndrome			
subjects affected / exposed	0 / 12 (0.00%)	1 / 83 (1.20%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune-mediated lung disease			
subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laryngeal oedema			

subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Restlessness			
subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Confusional state			
subjects affected / exposed	0 / 12 (0.00%)	1 / 83 (1.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bilirubin conjugated increased			
subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Platelet count decreased			
subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Transaminases increased			
subjects affected / exposed	0 / 12 (0.00%)	1 / 83 (1.20%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood corticotrophin decreased			
subjects affected / exposed	0 / 12 (0.00%)	1 / 83 (1.20%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood creatinine increased			
subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cortisol decreased			
subjects affected / exposed	0 / 12 (0.00%)	1 / 83 (1.20%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Infusion related reaction			
subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary radiation injury			
subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Radiation oesophagitis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rib fracture			
subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Toxicity to various agents			
subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anastomotic complication			
subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			
subjects affected / exposed	0 / 12 (0.00%)	1 / 83 (1.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bradycardia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac arrest			
subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure			
subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardio-respiratory arrest			
subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery disease			

subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic cardiomyopathy			
subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericardial effusion			
subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericarditis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Right ventricular failure			
subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Supraventricular tachycardia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute myocardial infarction			
subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Cerebral infarction			
subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrovascular accident			

subjects affected / exposed	0 / 12 (0.00%)	1 / 83 (1.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhagic stroke			
subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic stroke			
subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient ischaemic attack			
subjects affected / exposed	0 / 12 (0.00%)	1 / 83 (1.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brain injury			
subjects affected / exposed	0 / 12 (0.00%)	1 / 83 (1.20%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brown-Sequard syndrome			
subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral haemorrhage			
subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Encephalopathy			
subjects affected / exposed	0 / 12 (0.00%)	1 / 83 (1.20%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			

subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile neutropenia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Leukocytosis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancytopenia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombotic microangiopathy			
subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 12 (0.00%)	1 / 83 (1.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis			

subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Constipation			
subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	0 / 12 (0.00%)	3 / 83 (3.61%)	
occurrences causally related to treatment / all	0 / 0	3 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterocolitis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Faecaloma			
subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric ulcer			
subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastritis erosive			
subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			
subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis			

subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal obstruction			
subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stomatitis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastritis			
subjects affected / exposed	0 / 12 (0.00%)	1 / 83 (1.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal obstruction			
subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophagitis			
subjects affected / exposed	0 / 12 (0.00%)	1 / 83 (1.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oral lichen planus			
subjects affected / exposed	0 / 12 (0.00%)	1 / 83 (1.20%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Acute hepatic failure			

subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Autoimmune hepatitis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Lichenoid keratosis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rash			
subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lichen planus			
subjects affected / exposed	0 / 12 (0.00%)	1 / 83 (1.20%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rash maculo-papular			
subjects affected / exposed	0 / 12 (0.00%)	1 / 83 (1.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertensive nephropathy			
subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tubulointerstitial nephritis			

subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Hyperthyroidism			
subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypophysitis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Back pain			
subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteolysis			
subjects affected / exposed	0 / 12 (0.00%)	1 / 83 (1.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal pain			
subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematoma muscle			
subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Muscular weakness			
subjects affected / exposed	0 / 12 (0.00%)	1 / 83 (1.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium difficile colitis			
subjects affected / exposed	0 / 12 (0.00%)	2 / 83 (2.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis viral			
subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infectious pleural effusion			
subjects affected / exposed	0 / 12 (0.00%)	1 / 83 (1.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infective exacerbation of chronic obstructive airways disease			
subjects affected / exposed	0 / 12 (0.00%)	1 / 83 (1.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Lower respiratory tract infection			
subjects affected / exposed	0 / 12 (0.00%)	1 / 83 (1.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Neutropenic sepsis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oral candidiasis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritonsillar abscess			
subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	1 / 12 (8.33%)	2 / 83 (2.41%)	
occurrences causally related to treatment / all	0 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pulmonary sepsis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory tract infection			
subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	0 / 12 (0.00%)	1 / 83 (1.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic shock			

subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin infection			
subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Splenic abscess			
subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urosepsis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bursitis infective			
subjects affected / exposed	0 / 12 (0.00%)	1 / 83 (1.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Encephalomyelitis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymph gland infection			
subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningitis viral			

subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dehydration			
subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetes mellitus			
subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic ketoacidosis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypercalcaemia			
subjects affected / exposed	0 / 12 (0.00%)	1 / 83 (1.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypocalcaemia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperglycaemia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyponatraemia			

subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypovolaemia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fluid overload			
subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypokalaemia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Type 2 diabetes mellitus			
subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Pembrolizumab First Course	SOC Chemotherapy First Course	SOC Chemotherapy Switched over to Second Course Pembrolizumab
Total subjects affected by non-serious adverse events			
subjects affected / exposed	140 / 154 (90.91%)	142 / 150 (94.67%)	0 / 1 (0.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour pain			
subjects affected / exposed	1 / 154 (0.65%)	0 / 150 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Vascular disorders			
Hypertension			
subjects affected / exposed	11 / 154 (7.14%)	4 / 150 (2.67%)	0 / 1 (0.00%)
occurrences (all)	13	4	0

Hypotension			
subjects affected / exposed	4 / 154 (2.60%)	4 / 150 (2.67%)	0 / 1 (0.00%)
occurrences (all)	5	4	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	12 / 154 (7.79%)	17 / 150 (11.33%)	0 / 1 (0.00%)
occurrences (all)	17	30	0
Chest pain			
subjects affected / exposed	16 / 154 (10.39%)	16 / 150 (10.67%)	0 / 1 (0.00%)
occurrences (all)	17	16	0
Fatigue			
subjects affected / exposed	37 / 154 (24.03%)	53 / 150 (35.33%)	0 / 1 (0.00%)
occurrences (all)	45	93	0
Malaise			
subjects affected / exposed	6 / 154 (3.90%)	12 / 150 (8.00%)	0 / 1 (0.00%)
occurrences (all)	6	13	0
Oedema peripheral			
subjects affected / exposed	19 / 154 (12.34%)	15 / 150 (10.00%)	0 / 1 (0.00%)
occurrences (all)	20	19	0
Pyrexia			
subjects affected / exposed	27 / 154 (17.53%)	14 / 150 (9.33%)	0 / 1 (0.00%)
occurrences (all)	36	16	0
Influenza like illness			
subjects affected / exposed	2 / 154 (1.30%)	2 / 150 (1.33%)	0 / 1 (0.00%)
occurrences (all)	2	7	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	29 / 154 (18.83%)	21 / 150 (14.00%)	0 / 1 (0.00%)
occurrences (all)	44	24	0
Dyspnoea			
subjects affected / exposed	41 / 154 (26.62%)	24 / 150 (16.00%)	0 / 1 (0.00%)
occurrences (all)	50	29	0
Haemoptysis			
subjects affected / exposed	11 / 154 (7.14%)	5 / 150 (3.33%)	0 / 1 (0.00%)
occurrences (all)	11	5	0
Hiccups			

subjects affected / exposed	2 / 154 (1.30%)	10 / 150 (6.67%)	0 / 1 (0.00%)
occurrences (all)	2	12	0
Nasal congestion			
subjects affected / exposed	1 / 154 (0.65%)	2 / 150 (1.33%)	0 / 1 (0.00%)
occurrences (all)	1	2	0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	16 / 154 (10.39%)	11 / 150 (7.33%)	0 / 1 (0.00%)
occurrences (all)	18	11	0
Investigations			
Aspartate aminotransferase increased			
subjects affected / exposed	15 / 154 (9.74%)	7 / 150 (4.67%)	0 / 1 (0.00%)
occurrences (all)	19	9	0
Alanine aminotransferase increased			
subjects affected / exposed	17 / 154 (11.04%)	11 / 150 (7.33%)	0 / 1 (0.00%)
occurrences (all)	20	15	0
Blood alkaline phosphatase increased			
subjects affected / exposed	10 / 154 (6.49%)	4 / 150 (2.67%)	0 / 1 (0.00%)
occurrences (all)	14	4	0
Blood creatinine increased			
subjects affected / exposed	12 / 154 (7.79%)	21 / 150 (14.00%)	0 / 1 (0.00%)
occurrences (all)	15	26	0
Neutrophil count decreased			
subjects affected / exposed	1 / 154 (0.65%)	21 / 150 (14.00%)	0 / 1 (0.00%)
occurrences (all)	3	37	0
Platelet count decreased			
subjects affected / exposed	1 / 154 (0.65%)	19 / 150 (12.67%)	0 / 1 (0.00%)
occurrences (all)	1	28	0
White blood cell count decreased			
subjects affected / exposed	1 / 154 (0.65%)	17 / 150 (11.33%)	0 / 1 (0.00%)
occurrences (all)	3	25	0
Weight decreased			
subjects affected / exposed	14 / 154 (9.09%)	11 / 150 (7.33%)	0 / 1 (0.00%)
occurrences (all)	15	12	0
Injury, poisoning and procedural complications			

Eye injury			
subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Fall			
subjects affected / exposed	9 / 154 (5.84%)	4 / 150 (2.67%)	0 / 1 (0.00%)
occurrences (all)	9	4	0
Ligament sprain			
subjects affected / exposed	2 / 154 (1.30%)	1 / 150 (0.67%)	0 / 1 (0.00%)
occurrences (all)	2	1	0
Cardiac disorders			
Bradycardia			
subjects affected / exposed	1 / 154 (0.65%)	1 / 150 (0.67%)	0 / 1 (0.00%)
occurrences (all)	1	1	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	20 / 154 (12.99%)	12 / 150 (8.00%)	0 / 1 (0.00%)
occurrences (all)	25	16	0
Dysgeusia			
subjects affected / exposed	2 / 154 (1.30%)	13 / 150 (8.67%)	0 / 1 (0.00%)
occurrences (all)	2	13	0
Headache			
subjects affected / exposed	11 / 154 (7.14%)	7 / 150 (4.67%)	0 / 1 (0.00%)
occurrences (all)	17	8	0
Neuropathy peripheral			
subjects affected / exposed	2 / 154 (1.30%)	10 / 150 (6.67%)	0 / 1 (0.00%)
occurrences (all)	2	10	0
Tremor			
subjects affected / exposed	1 / 154 (0.65%)	2 / 150 (1.33%)	0 / 1 (0.00%)
occurrences (all)	1	2	0
Blood and lymphatic system disorders			
Leukopenia			
subjects affected / exposed	1 / 154 (0.65%)	10 / 150 (6.67%)	0 / 1 (0.00%)
occurrences (all)	1	17	0
Neutropenia			
subjects affected / exposed	2 / 154 (1.30%)	35 / 150 (23.33%)	0 / 1 (0.00%)
occurrences (all)	4	67	0
Anaemia			

subjects affected / exposed	24 / 154 (15.58%)	77 / 150 (51.33%)	0 / 1 (0.00%)
occurrences (all)	28	98	0
Thrombocytopenia			
subjects affected / exposed	2 / 154 (1.30%)	18 / 150 (12.00%)	0 / 1 (0.00%)
occurrences (all)	2	32	0
Eye disorders			
Conjunctivitis allergic			
subjects affected / exposed	1 / 154 (0.65%)	0 / 150 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	14 / 154 (9.09%)	10 / 150 (6.67%)	0 / 1 (0.00%)
occurrences (all)	17	10	0
Constipation			
subjects affected / exposed	35 / 154 (22.73%)	33 / 150 (22.00%)	0 / 1 (0.00%)
occurrences (all)	43	54	0
Diarrhoea			
subjects affected / exposed	41 / 154 (26.62%)	33 / 150 (22.00%)	0 / 1 (0.00%)
occurrences (all)	65	43	0
Dyspepsia			
subjects affected / exposed	6 / 154 (3.90%)	9 / 150 (6.00%)	0 / 1 (0.00%)
occurrences (all)	7	14	0
Nausea			
subjects affected / exposed	33 / 154 (21.43%)	68 / 150 (45.33%)	0 / 1 (0.00%)
occurrences (all)	44	129	0
Stomatitis			
subjects affected / exposed	8 / 154 (5.19%)	17 / 150 (11.33%)	0 / 1 (0.00%)
occurrences (all)	8	23	0
Vomiting			
subjects affected / exposed	16 / 154 (10.39%)	36 / 150 (24.00%)	0 / 1 (0.00%)
occurrences (all)	20	65	0
Abdominal pain upper			
subjects affected / exposed	7 / 154 (4.55%)	7 / 150 (4.67%)	0 / 1 (0.00%)
occurrences (all)	9	13	0
Dysphagia			

subjects affected / exposed	2 / 154 (1.30%)	6 / 150 (4.00%)	0 / 1 (0.00%)
occurrences (all)	2	6	0
Oesophagitis			
subjects affected / exposed	1 / 154 (0.65%)	1 / 150 (0.67%)	0 / 1 (0.00%)
occurrences (all)	1	1	0
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	2 / 154 (1.30%)	15 / 150 (10.00%)	0 / 1 (0.00%)
occurrences (all)	2	15	0
Dry skin			
subjects affected / exposed	17 / 154 (11.04%)	1 / 150 (0.67%)	0 / 1 (0.00%)
occurrences (all)	18	1	0
Pruritus			
subjects affected / exposed	32 / 154 (20.78%)	6 / 150 (4.00%)	0 / 1 (0.00%)
occurrences (all)	46	6	0
Rash			
subjects affected / exposed	28 / 154 (18.18%)	7 / 150 (4.67%)	0 / 1 (0.00%)
occurrences (all)	43	8	0
Panniculitis			
subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Rash maculo-papular			
subjects affected / exposed	7 / 154 (4.55%)	1 / 150 (0.67%)	0 / 1 (0.00%)
occurrences (all)	8	2	0
Endocrine disorders			
Hyperthyroidism			
subjects affected / exposed	10 / 154 (6.49%)	2 / 150 (1.33%)	0 / 1 (0.00%)
occurrences (all)	11	3	0
Hypothyroidism			
subjects affected / exposed	16 / 154 (10.39%)	3 / 150 (2.00%)	0 / 1 (0.00%)
occurrences (all)	16	3	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	34 / 154 (22.08%)	17 / 150 (11.33%)	0 / 1 (0.00%)
occurrences (all)	47	21	0
Back pain			

subjects affected / exposed	23 / 154 (14.94%)	18 / 150 (12.00%)	0 / 1 (0.00%)
occurrences (all)	26	21	0
Muscle spasms			
subjects affected / exposed	10 / 154 (6.49%)	2 / 150 (1.33%)	0 / 1 (0.00%)
occurrences (all)	10	2	0
Pain in extremity			
subjects affected / exposed	9 / 154 (5.84%)	10 / 150 (6.67%)	0 / 1 (0.00%)
occurrences (all)	12	13	0
Myalgia			
subjects affected / exposed	10 / 154 (6.49%)	2 / 150 (1.33%)	0 / 1 (0.00%)
occurrences (all)	11	2	0
Periarthritis			
subjects affected / exposed	0 / 154 (0.00%)	0 / 150 (0.00%)	0 / 1 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	11 / 154 (7.14%)	5 / 150 (3.33%)	0 / 1 (0.00%)
occurrences (all)	18	7	0
Nasopharyngitis			
subjects affected / exposed	18 / 154 (11.69%)	2 / 150 (1.33%)	0 / 1 (0.00%)
occurrences (all)	27	2	0
Bronchitis			
subjects affected / exposed	8 / 154 (5.19%)	4 / 150 (2.67%)	0 / 1 (0.00%)
occurrences (all)	9	5	0
Infected dermal cyst			
subjects affected / exposed	1 / 154 (0.65%)	0 / 150 (0.00%)	0 / 1 (0.00%)
occurrences (all)	1	0	0
Influenza			
subjects affected / exposed	2 / 154 (1.30%)	2 / 150 (1.33%)	0 / 1 (0.00%)
occurrences (all)	2	3	0
Tooth infection			
subjects affected / exposed	2 / 154 (1.30%)	2 / 150 (1.33%)	0 / 1 (0.00%)
occurrences (all)	2	2	0
Sinusitis			
subjects affected / exposed	2 / 154 (1.30%)	2 / 150 (1.33%)	0 / 1 (0.00%)
occurrences (all)	2	2	0

Urinary tract infection			
subjects affected / exposed	9 / 154 (5.84%)	8 / 150 (5.33%)	0 / 1 (0.00%)
occurrences (all)	11	11	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	33 / 154 (21.43%)	49 / 150 (32.67%)	0 / 1 (0.00%)
occurrences (all)	36	71	0
Hyperglycaemia			
subjects affected / exposed	10 / 154 (6.49%)	9 / 150 (6.00%)	0 / 1 (0.00%)
occurrences (all)	17	10	0
Hypomagnesaemia			
subjects affected / exposed	4 / 154 (2.60%)	13 / 150 (8.67%)	0 / 1 (0.00%)
occurrences (all)	7	18	0
Hyponatraemia			
subjects affected / exposed	11 / 154 (7.14%)	12 / 150 (8.00%)	0 / 1 (0.00%)
occurrences (all)	17	13	0
Hyperkalaemia			
subjects affected / exposed	8 / 154 (5.19%)	6 / 150 (4.00%)	0 / 1 (0.00%)
occurrences (all)	9	7	0
Hypoalbuminaemia			
subjects affected / exposed	8 / 154 (5.19%)	7 / 150 (4.67%)	0 / 1 (0.00%)
occurrences (all)	8	7	0

Non-serious adverse events	Pembrolizumab Second Course	SOC Chemotherapy Switched Over to Pembrolizumab First Course	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	10 / 12 (83.33%)	72 / 83 (86.75%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour pain			
subjects affected / exposed	1 / 12 (8.33%)	0 / 83 (0.00%)	
occurrences (all)	1	0	
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences (all)	0	0	
Hypotension			

subjects affected / exposed	1 / 12 (8.33%)	2 / 83 (2.41%)	
occurrences (all)	1	2	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 12 (0.00%)	7 / 83 (8.43%)	
occurrences (all)	0	7	
Chest pain			
subjects affected / exposed	0 / 12 (0.00%)	5 / 83 (6.02%)	
occurrences (all)	0	6	
Fatigue			
subjects affected / exposed	1 / 12 (8.33%)	18 / 83 (21.69%)	
occurrences (all)	1	19	
Malaise			
subjects affected / exposed	0 / 12 (0.00%)	1 / 83 (1.20%)	
occurrences (all)	0	2	
Oedema peripheral			
subjects affected / exposed	0 / 12 (0.00%)	3 / 83 (3.61%)	
occurrences (all)	0	4	
Pyrexia			
subjects affected / exposed	0 / 12 (0.00%)	8 / 83 (9.64%)	
occurrences (all)	0	8	
Influenza like illness			
subjects affected / exposed	1 / 12 (8.33%)	3 / 83 (3.61%)	
occurrences (all)	1	4	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 12 (8.33%)	16 / 83 (19.28%)	
occurrences (all)	1	17	
Dyspnoea			
subjects affected / exposed	0 / 12 (0.00%)	9 / 83 (10.84%)	
occurrences (all)	0	10	
Haemoptysis			
subjects affected / exposed	1 / 12 (8.33%)	7 / 83 (8.43%)	
occurrences (all)	1	10	
Hiccups			

subjects affected / exposed	0 / 12 (0.00%)	1 / 83 (1.20%)	
occurrences (all)	0	1	
Nasal congestion			
subjects affected / exposed	1 / 12 (8.33%)	3 / 83 (3.61%)	
occurrences (all)	1	3	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 12 (0.00%)	7 / 83 (8.43%)	
occurrences (all)	0	7	
Investigations			
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 12 (8.33%)	4 / 83 (4.82%)	
occurrences (all)	1	4	
Alanine aminotransferase increased			
subjects affected / exposed	1 / 12 (8.33%)	4 / 83 (4.82%)	
occurrences (all)	1	4	
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 12 (8.33%)	2 / 83 (2.41%)	
occurrences (all)	1	2	
Blood creatinine increased			
subjects affected / exposed	0 / 12 (0.00%)	5 / 83 (6.02%)	
occurrences (all)	0	9	
Neutrophil count decreased			
subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences (all)	0	0	
Platelet count decreased			
subjects affected / exposed	0 / 12 (0.00%)	1 / 83 (1.20%)	
occurrences (all)	0	1	
White blood cell count decreased			
subjects affected / exposed	1 / 12 (8.33%)	1 / 83 (1.20%)	
occurrences (all)	1	1	
Weight decreased			
subjects affected / exposed	2 / 12 (16.67%)	6 / 83 (7.23%)	
occurrences (all)	2	8	
Injury, poisoning and procedural complications			

Eye injury			
subjects affected / exposed	1 / 12 (8.33%)	0 / 83 (0.00%)	
occurrences (all)	1	0	
Fall			
subjects affected / exposed	0 / 12 (0.00%)	3 / 83 (3.61%)	
occurrences (all)	0	5	
Ligament sprain			
subjects affected / exposed	1 / 12 (8.33%)	0 / 83 (0.00%)	
occurrences (all)	1	0	
Cardiac disorders			
Bradycardia			
subjects affected / exposed	1 / 12 (8.33%)	0 / 83 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 12 (0.00%)	5 / 83 (6.02%)	
occurrences (all)	0	7	
Dysgeusia			
subjects affected / exposed	0 / 12 (0.00%)	1 / 83 (1.20%)	
occurrences (all)	0	1	
Headache			
subjects affected / exposed	0 / 12 (0.00%)	7 / 83 (8.43%)	
occurrences (all)	0	7	
Neuropathy peripheral			
subjects affected / exposed	0 / 12 (0.00%)	3 / 83 (3.61%)	
occurrences (all)	0	3	
Tremor			
subjects affected / exposed	1 / 12 (8.33%)	0 / 83 (0.00%)	
occurrences (all)	1	0	
Blood and lymphatic system disorders			
Leukopenia			
subjects affected / exposed	1 / 12 (8.33%)	0 / 83 (0.00%)	
occurrences (all)	1	0	
Neutropenia			
subjects affected / exposed	1 / 12 (8.33%)	1 / 83 (1.20%)	
occurrences (all)	1	1	
Anaemia			

subjects affected / exposed	0 / 12 (0.00%)	4 / 83 (4.82%)	
occurrences (all)	0	4	
Thrombocytopenia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 83 (0.00%)	
occurrences (all)	0	0	
Eye disorders			
Conjunctivitis allergic			
subjects affected / exposed	1 / 12 (8.33%)	1 / 83 (1.20%)	
occurrences (all)	1	1	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 12 (8.33%)	7 / 83 (8.43%)	
occurrences (all)	1	7	
Constipation			
subjects affected / exposed	2 / 12 (16.67%)	7 / 83 (8.43%)	
occurrences (all)	2	7	
Diarrhoea			
subjects affected / exposed	1 / 12 (8.33%)	18 / 83 (21.69%)	
occurrences (all)	1	22	
Dyspepsia			
subjects affected / exposed	1 / 12 (8.33%)	3 / 83 (3.61%)	
occurrences (all)	2	3	
Nausea			
subjects affected / exposed	1 / 12 (8.33%)	15 / 83 (18.07%)	
occurrences (all)	1	19	
Stomatitis			
subjects affected / exposed	0 / 12 (0.00%)	3 / 83 (3.61%)	
occurrences (all)	0	3	
Vomiting			
subjects affected / exposed	0 / 12 (0.00%)	8 / 83 (9.64%)	
occurrences (all)	0	9	
Abdominal pain upper			
subjects affected / exposed	1 / 12 (8.33%)	2 / 83 (2.41%)	
occurrences (all)	1	2	
Dysphagia			

subjects affected / exposed	1 / 12 (8.33%)	3 / 83 (3.61%)	
occurrences (all)	1	3	
Oesophagitis			
subjects affected / exposed	1 / 12 (8.33%)	0 / 83 (0.00%)	
occurrences (all)	1	0	
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	0 / 12 (0.00%)	2 / 83 (2.41%)	
occurrences (all)	0	2	
Dry skin			
subjects affected / exposed	1 / 12 (8.33%)	7 / 83 (8.43%)	
occurrences (all)	1	7	
Pruritus			
subjects affected / exposed	2 / 12 (16.67%)	13 / 83 (15.66%)	
occurrences (all)	2	13	
Rash			
subjects affected / exposed	0 / 12 (0.00%)	8 / 83 (9.64%)	
occurrences (all)	0	13	
Panniculitis			
subjects affected / exposed	1 / 12 (8.33%)	0 / 83 (0.00%)	
occurrences (all)	1	0	
Rash maculo-papular			
subjects affected / exposed	0 / 12 (0.00%)	6 / 83 (7.23%)	
occurrences (all)	0	6	
Endocrine disorders			
Hyperthyroidism			
subjects affected / exposed	0 / 12 (0.00%)	5 / 83 (6.02%)	
occurrences (all)	0	7	
Hypothyroidism			
subjects affected / exposed	1 / 12 (8.33%)	8 / 83 (9.64%)	
occurrences (all)	1	8	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 12 (0.00%)	16 / 83 (19.28%)	
occurrences (all)	0	18	
Back pain			

subjects affected / exposed	0 / 12 (0.00%)	4 / 83 (4.82%)	
occurrences (all)	0	4	
Muscle spasms			
subjects affected / exposed	0 / 12 (0.00%)	2 / 83 (2.41%)	
occurrences (all)	0	3	
Pain in extremity			
subjects affected / exposed	1 / 12 (8.33%)	6 / 83 (7.23%)	
occurrences (all)	1	8	
Myalgia			
subjects affected / exposed	0 / 12 (0.00%)	5 / 83 (6.02%)	
occurrences (all)	0	5	
Periarthritis			
subjects affected / exposed	1 / 12 (8.33%)	0 / 83 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	4 / 12 (33.33%)	9 / 83 (10.84%)	
occurrences (all)	4	12	
Nasopharyngitis			
subjects affected / exposed	2 / 12 (16.67%)	9 / 83 (10.84%)	
occurrences (all)	2	10	
Bronchitis			
subjects affected / exposed	0 / 12 (0.00%)	5 / 83 (6.02%)	
occurrences (all)	0	6	
Infected dermal cyst			
subjects affected / exposed	1 / 12 (8.33%)	0 / 83 (0.00%)	
occurrences (all)	1	0	
Influenza			
subjects affected / exposed	1 / 12 (8.33%)	1 / 83 (1.20%)	
occurrences (all)	1	1	
Tooth infection			
subjects affected / exposed	1 / 12 (8.33%)	2 / 83 (2.41%)	
occurrences (all)	1	3	
Sinusitis			
subjects affected / exposed	1 / 12 (8.33%)	2 / 83 (2.41%)	
occurrences (all)	1	2	

Urinary tract infection			
subjects affected / exposed	0 / 12 (0.00%)	4 / 83 (4.82%)	
occurrences (all)	0	4	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	2 / 12 (16.67%)	12 / 83 (14.46%)	
occurrences (all)	2	13	
Hyperglycaemia			
subjects affected / exposed	0 / 12 (0.00%)	2 / 83 (2.41%)	
occurrences (all)	0	3	
Hypomagnesaemia			
subjects affected / exposed	1 / 12 (8.33%)	5 / 83 (6.02%)	
occurrences (all)	1	5	
Hyponatraemia			
subjects affected / exposed	0 / 12 (0.00%)	7 / 83 (8.43%)	
occurrences (all)	0	8	
Hyperkalaemia			
subjects affected / exposed	0 / 12 (0.00%)	3 / 83 (3.61%)	
occurrences (all)	0	4	
Hypoalbuminaemia			
subjects affected / exposed	0 / 12 (0.00%)	3 / 83 (3.61%)	
occurrences (all)	0	6	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
21 October 2014	The primary reasons for amendment 1 were to incorporate input from regulatory authorities, changed the length of the trial from 2.5 to 3 years, MK-3475 was changed to pembrolizumab, optional KRAS testing was removed, total administration of pembrolizumab was changed from 2 years to 35 cycles and the second course was limited to 1 year.
28 January 2016	The primary reason for amendment 3 was to incorporate an addition of an interim efficacy analysis for an external DMC review.
02 August 2016	The primary reason for amendment 6 was the removal of the requirement for documented disease progression in order to crossover to pembrolizumab.
18 January 2018	The primary reasons for amendment 9 was to allow flexibility of survival status activities and to provide current, comprehensive guidelines for the management of immune-related adverse events.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported