



Clinical trial results:

A Phase III Study of Pembrolizumab (MK-3475) vs. Chemotherapy in Microsatellite Instability-High (MSI-H) or Mismatch Repair Deficient (dMMR) Stage IV Colorectal Carcinoma (KEYNOTE-177)

Summary

EudraCT number	2015-002024-89
Trial protocol	ES DE FI SE IE DK NL FR IT BE
Global end of trial date	17 July 2023

Results information

Result version number	v1 (current)
This version publication date	13 July 2024
First version publication date	13 July 2024

Trial information

Trial identification

Sponsor protocol code	3475-177
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02563002
WHO universal trial number (UTN)	-
Other trial identifiers	Merck: KEYNOTE-177

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	17 July 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	19 February 2021
Global end of trial reached?	Yes
Global end of trial date	17 July 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

In this study, participants with stage IV Microsatellite Instability-High (MSI-H) or Mismatch Repair Deficient (dMMR) colorectal carcinoma (CRC) will be randomly assigned to receive either pembrolizumab or the Investigator's choice of 1 of 6 standard of care (SOC) chemotherapy regimens for the treatment of advanced colorectal carcinoma. The primary study hypothesis is that pembrolizumab will prolong progression-free survival (PFS) or overall survival (OS) compared to current SOC chemotherapy.

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	30 November 2015
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	United Kingdom: 20
Country: Number of subjects enrolled	United States: 55
Country: Number of subjects enrolled	Australia: 13
Country: Number of subjects enrolled	Belgium: 4
Country: Number of subjects enrolled	Brazil: 12
Country: Number of subjects enrolled	Canada: 6
Country: Number of subjects enrolled	Denmark: 22
Country: Number of subjects enrolled	Finland: 5
Country: Number of subjects enrolled	France: 36
Country: Number of subjects enrolled	Germany: 6
Country: Number of subjects enrolled	Ireland: 4
Country: Number of subjects enrolled	Israel: 8
Country: Number of subjects enrolled	Italy: 2
Country: Number of subjects enrolled	Japan: 22
Country: Number of subjects enrolled	Korea, Republic of: 14
Country: Number of subjects enrolled	Netherlands: 14
Country: Number of subjects enrolled	Norway: 9
Country: Number of subjects enrolled	Singapore: 5

Country: Number of subjects enrolled	South Africa: 4
Country: Number of subjects enrolled	Spain: 29
Country: Number of subjects enrolled	Sweden: 4
Country: Number of subjects enrolled	Switzerland: 6
Country: Number of subjects enrolled	Taiwan: 7
Worldwide total number of subjects	307
EEA total number of subjects	135

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)	163
From 65 to 84 years	129
85 years and over	15

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Of the 307 participants randomized in the study, 296 participants received study medication and were evaluable for safety analyses.

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 intravenously (IV) on Day 1 of each 21-day cycle (Q3W) for up to 35 treatments (approximately 2 years). Eligible participants who stopped the initial course of pembrolizumab due to complete response (CR) or completed initial course of pembrolizumab and had stable disease but progressed after discontinuation, initiated a second course of pembrolizumab at the investigator's discretion for up to 17 cycles (approximately 1 year additional).

Arm type	Experimental
Investigational medicinal product name	Pembrolizumab
Investigational medicinal product code	
Other name	MK-3475 SCH 90047 5KEYTRUDA®
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Pembrolizumab 200 mg intravenously (IV) on Day 1 of each 21-day cycle (Q3W) for up to 35 treatments (approximately 2 years).

Arm title	Standard of Care (SOC)
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Arm description:

Participants received 1 of 6 possible standard chemotherapy regimens: mFOLFOX6, or mFOLFOX6+bevacizumab 5 mg/kg IV on Day 1 of each 2-week cycle, or mFOLFOX6+cetuximab 400 mg/m² IV over 2 hours then 250 mg/m² over 1 hour weekly in each 2-week cycle, or FOLFIRI, or FOLFIRI+bevacizumab 5 mg/kg IV on Day 1 of each 2-week cycle, or FOLFIRI+cetuximab 400 mg/m² IV over 2 hours then 250 mg/m² over 1 hour weekly in each 2-week cycle. Participants with documented disease progression following chemotherapy can crossover to receive pembrolizumab for up to 35 cycles (approximately 2 years). Eligible cross over participants who stopped pembrolizumab who stopped pembrolizumab and had stable disease but progressed after discontinuation, initiated a second course of pembrolizumab at the investigator's discretion for up to 17 cycles (approximately 1 year additional).

Arm type	Active comparator
Investigational medicinal product name	mFOLFOX6
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Regimen consists of oxaliplatin 85 mg/m² IV on Day 1, leucovorin 400 mg/m² or levoleucovorin 200 mg/m² IV on Day 1, 5-fluorouracil (5-FU) 400 mg/m² IV bolus on Day 1 and then 1200 mg/m²/day IV over 2 days for total dose of 2400 mg/m² in each 2-week cycle.

Investigational medicinal product name	Cetuximab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use
Dosage and administration details:	
Cetuximab 400 mg/ m ² IV over 2 hours first infusion, then 250mg/m ² IV over 1 hour weekly.	
Investigational medicinal product name	Bevacizumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use
Dosage and administration details:	
Bevacizumab 5 mg/kg IV on Day 1, every 2 weeks	
Investigational medicinal product name	FOLFIRI
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use
Dosage and administration details:	
Regimen consists of oxaliplatin 85 mg/m ² IV on Day 1, leucovorin 400 mg/m ² or levoleucovorin 200 mg/m ² IV on Day 1, 5-fluorouracil (5-FU) 400 mg/m ² IV bolus on Day 1 and then 1200 mg/m ² /day IV over 2 days for total dose of 2400 mg/m ² in each 2-week cycle.	

Number of subjects in period 1	Pembrolizumab	Standard of Care (SOC)
Started	153	154
Treated	153	143
Received Second Course of Pembrolizumab	12	5
Switched over to Pembrolizumab	0	7
Completed	0	0
Not completed	153	154
Adverse event, serious fatal	72	87
Consent withdrawn by subject	2	10
Physician decision	-	2
Lost to follow-up	5	-
Sponsor decision	74	55

Baseline characteristics

Reporting groups

Reporting group title	Pembrolizumab
Reporting group description:	
Participants received pembrolizumab 200 mg intravenously (IV) on Day 1 of each 21-day cycle (Q3W) for up to 35 treatments (approximately 2 years). Eligible participants who stopped the initial course of pembrolizumab due to complete response (CR) or completed initial course of pembrolizumab and had stable disease but progressed after discontinuation, initiated a second course of pembrolizumab at the investigator's discretion for up to 17 cycles (approximately 1 year additional).	
Reporting group title	Standard of Care (SOC)
Reporting group description:	
Participants received 1 of 6 possible standard chemotherapy regimens: mFOLFOX6, or mFOLFOX6+bevacizumab 5 mg/kg IV on Day 1 of each 2-week cycle, or mFOLFOX6+cetuximab 400 mg/m ² IV over 2 hours then 250 mg/m ² over 1 hour weekly in each 2-week cycle, or FOLFIRI, or FOLFIRI+bevacizumab 5 mg/kg IV on Day 1 of each 2-week cycle, or FOLFIRI+cetuximab 400 mg/m ² IV over 2 hours then 250 mg/m ² over 1 hour weekly in each 2-week cycle. Participants with documented disease progression following chemotherapy can crossover to receive pembrolizumab for up to 35 cycles (approximately 2 years). Eligible cross over participants who stopped pembrolizumab who stopped pembrolizumab and had stable disease but progressed after discontinuation, initiated a second course of pembrolizumab at the investigator's discretion for up to 17 cycles (approximately 1 year additional).	

Reporting group values	Pembrolizumab	Standard of Care (SOC)	Total
Number of subjects	153	154	307
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age Continuous Units: Years			
arithmetic mean standard deviation	61.9 ± 14.9	60.6 ± 14.8	-
Sex: Female, Male Units: Participants			
Female	82	72	154
Male	71	82	153
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	24	26	50
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	9	5	14

White	113	116	229
More than one race	0	0	0
Unknown or Not Reported	7	7	14
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	11	10	21
Not Hispanic or Latino	128	131	259
Unknown or Not Reported	14	13	27

End points

End points reporting groups

Reporting group title	Pembrolizumab
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Reporting group description:

Participants received pembrolizumab 200 mg intravenously (IV) on Day 1 of each 21-day cycle (Q3W) for up to 35 treatments (approximately 2 years). Eligible participants who stopped the initial course of pembrolizumab due to complete response (CR) or completed initial course of pembrolizumab and had stable disease but progressed after discontinuation, initiated a second course of pembrolizumab at the investigator's discretion for up to 17 cycles (approximately 1 year additional).

Reporting group title	Standard of Care (SOC)
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Reporting group description:

Participants received 1 of 6 possible standard chemotherapy regimens: mFOLFOX6, or mFOLFOX6+bevacizumab 5 mg/kg IV on Day 1 of each 2-week cycle, or mFOLFOX6+cetuximab 400 mg/m² IV over 2 hours then 250 mg/m² over 1 hour weekly in each 2-week cycle, or FOLFIRI, or FOLFIRI+bevacizumab 5 mg/kg IV on Day 1 of each 2-week cycle, or FOLFIRI+cetuximab 400 mg/m² IV over 2 hours then 250 mg/m² over 1 hour weekly in each 2-week cycle. Participants with documented disease progression following chemotherapy can crossover to receive pembrolizumab for up to 35 cycles (approximately 2 years). Eligible cross over participants who stopped pembrolizumab who stopped pembrolizumab and had stable disease but progressed after discontinuation, initiated a second course of pembrolizumab at the investigator's discretion for up to 17 cycles (approximately 1 year additional).

Primary: Progression-Free Survival (PFS) per RECIST1.1 As Assessed by Central Imaging Vendor

End point title	Progression-Free Survival (PFS) per RECIST1.1 As Assessed by Central Imaging Vendor
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End point description:

PFS was defined as the time from randomization to the first documented disease progression (PD) per RECIST 1.1 based on blinded central imaging vendor review or death due to any cause, whichever occurs first. Per RECIST 1.1, PD was defined as $\geq 20\%$ increase in the sum of diameters of target lesions. In addition to the relative increase of 20%, the sum had to demonstrate an absolute increase of ≥ 5 mm. The appearance of one or more new lesions was also considered PD. Hazards ratio (HR) and associated 95% confidence intervals (CIs) from a Cox proportional hazard model with Efron's method of tie handling and with a single treatment covariate was presented for the first course study treatment per protocol. The analysis population included all randomized participants.

End point type	Primary
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End point timeframe:

Up to approximately 59 months

End point values	Pembrolizumab	Standard of Care (SOC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	153	154		
Units: Months				
median (confidence interval 95%)	16.5 (5.4 to 38.1)	8.2 (6.1 to 10.2)		

Statistical analyses

Statistical analysis title	Hazard Ratio
Comparison groups	Pembrolizumab v Standard of Care (SOC)
Number of subjects included in analysis	307
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0001
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.59
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.45
upper limit	0.79

Primary: Overall Survival (OS)

End point title	Overall Survival (OS)
End point description:	
OS was defined as the time from randomization to death due to any cause. Participants without documented death at the time of analysis were censored at the date of last known contact. HR and associated 95% CIs from a Cox proportional hazard model with Efron's method of tie handling and with a single treatment covariate was presented for the first course study treatment per protocol. The analysis population included all randomized participants.	
End point type	Primary
End point timeframe:	
Up to approximately 59 months	

End point values	Pembrolizumab	Standard of Care (SOC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	153	154		
Units: Months				
median (confidence interval 95%)	9999 (49.2 to 9999)	36.7 (27.6 to 9999)		

Statistical analyses

Statistical analysis title	Hazards Ratio
Comparison groups	Pembrolizumab v Standard of Care (SOC)

Number of subjects included in analysis	307
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0359
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.74
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.53
upper limit	1.03

Secondary: Overall Response Rate (ORR) per RECIST1.1 as Assessed by Central Imaging Vendor

End point title	Overall Response Rate (ORR) per RECIST1.1 as Assessed by Central Imaging Vendor
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End point description:

ORR was defined as the percentage of the participants 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 as assessed by the central imaging vendor. The percentage of participants who experienced a CR or PR was presented for the first course of study treatment per protocol. The analysis population included all randomized participants.

End point type	Secondary
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End point timeframe:

Up to approximately 59 months

End point values	Pembrolizumab	Standard of Care (SOC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	153	154		
Units: Percentage of Participants				
number (confidence interval 95%)	45.1 (37.1 to 53.3)	33.1 (25.8 to 41.1)		

Statistical analyses

Statistical analysis title	Estimated difference in percentage
Comparison groups	Pembrolizumab v Standard of Care (SOC)
Number of subjects included in analysis	307
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0159 ^[1]
Method	Miettinen & Nurminen method
Parameter estimate	Difference in percentage
Point estimate	12

Confidence interval	
level	95 %
sides	2-sided
lower limit	1
upper limit	22.6

Notes:

[1] - One-sided p-value based on Miettinen & Nurminen method.

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

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

An AE was defined as any untoward medical occurrence in a participant or clinical investigation participant administered a study treatment and which does not necessarily have to have a causal relationship with this treatment. An AE could be any unfavourable and unintended sign (including an abnormal laboratory finding, for example), symptom, or disease temporally associated with the use of a study treatment, whether or not considered related to the study treatment. Any worsening (i.e., any clinically significant adverse change infrequency and/or intensity) of a preexisting condition that was temporally associated with the use of study treatment, was also an AE. The number of participants who experienced at least one AE was presented for the first course study treatment per protocol. The analysis population included all randomized participants who received at least 1 dose of study treatment.

End point type	Secondary
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End point timeframe:

Up to approximately 59 months

End point values	Pembrolizumab	Standard of Care (SOC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	153	143		
Units: Participants	149	142		

Statistical analyses

No statistical analyses for this end point

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

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

An AE was defined as any untoward medical occurrence in a participant or clinical investigation participant administered a study treatment and which does not necessarily have to have a causal relationship with this treatment. An AE could be any unfavourable and unintended sign (including an abnormal laboratory finding, for example), symptom, or disease temporally associated with the use of a study treatment, whether or not considered related to the study treatment. Any worsening (i.e., any clinically significant adverse change infrequency and/or intensity) of a preexisting condition that was temporally associated with the use of study treatment, was also an AE. The number of participants who discontinued study treatment due to an AE was presented for the first course study treatment per protocol. The analysis population included all randomized participants who received at least 1 dose of study treatment.

End point type	Secondary
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End point timeframe:

Up to approximately 59 months

End point values	Pembrolizumab	Standard of Care (SOC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	153	143		
Units: Participants	21	20		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to approximately 91 months

Adverse event reporting additional description:

All-cause mortality=all randomized participants (n=307) & adverse events (AEs)=participants who received ≥ 1 dose of study treatment. MedDRA terms neoplasm progression (NP), malignant NP, & disease progression unrelated to treatment were excluded. Per protocol, first & second course AEs were reported.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	26.0
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Reporting groups

Reporting group title	Pembrolizumab First Course
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Reporting group description:

Participants received pembrolizumab 200 mg intravenously (IV) on Day 1 of each 21-day cycle (Q3W) for up to 35 treatments (approximately 2 years).

Reporting group title	SOC First Course
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Reporting group description:

Participants received 1 of 6 possible standard chemotherapy regimens: mFOLFOX6, or mFOLFOX6+bevacizumab 5 mg/kg IV on Day 1 of each 2-week cycle, or mFOLFOX6+cetuximab 400 mg/m² IV over 2 hours then 250 mg/m² over 1 hour weekly in each 2-week cycle, or FOLFIRI, or FOLFIRI+bevacizumab 5 mg/kg IV on Day 1 of each 2-week cycle, or FOLFIRI+cetuximab 400 mg/m² IV over 2 hours then 250 mg/m² over 1 hour weekly in each 2-week cycle.

Reporting group title	SOC Crossed over to Pembrolizumab
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Reporting group description:

Eligible participants with documented disease progression following chemotherapy in SOC arm switched over to receive pembrolizumab for up to 35 cycles (approximately 2 years).

Reporting group title	Pembrolizumab Second Course
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Reporting group description:

Participants who received pembrolizumab as a first course and stopped the first course of pembrolizumab due to complete response (CR) or completed the first course of pembrolizumab and had stable disease but progressed after discontinuation, initiated a second course of pembrolizumab at the investigator's discretion for up to 17 cycles (approximately 1 year additional).

Reporting group title	SOC Crossed over to Pembrolizumab Second Course
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Reporting group description:

Participants who switched over from SOC and received pembrolizumab and subsequently stopped the first course of pembrolizumab due to complete response (CR) or completed the first course of pembrolizumab and had stable disease but progressed after discontinuation, initiated a second course of pembrolizumab at the investigator's discretion for up to 17 cycles (approximately 1 year additional).

Serious adverse events	Pembrolizumab First Course	SOC First Course	SOC Crossed over to Pembrolizumab
Total subjects affected by serious adverse events			
subjects affected / exposed	62 / 153 (40.52%)	76 / 143 (53.15%)	27 / 57 (47.37%)
number of deaths (all causes)	68	58	30
number of deaths resulting from adverse events	6	7	5
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			

Basal cell carcinoma			
subjects affected / exposed	1 / 153 (0.65%)	0 / 143 (0.00%)	1 / 57 (1.75%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bladder neoplasm			
subjects affected / exposed	1 / 153 (0.65%)	0 / 143 (0.00%)	0 / 57 (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
Breast cancer			
subjects affected / exposed	1 / 153 (0.65%)	0 / 143 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Squamous cell carcinoma			
subjects affected / exposed	2 / 153 (1.31%)	0 / 143 (0.00%)	1 / 57 (1.75%)
occurrences causally related to treatment / all	2 / 4	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal neoplasm			
subjects affected / exposed	0 / 153 (0.00%)	1 / 143 (0.70%)	0 / 57 (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
Oropharyngeal cancer			
subjects affected / exposed	0 / 153 (0.00%)	0 / 143 (0.00%)	1 / 57 (1.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Lung carcinoma cell type unspecified recurrent			
subjects affected / exposed	0 / 153 (0.00%)	0 / 143 (0.00%)	1 / 57 (1.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Infected neoplasm			
subjects affected / exposed	1 / 153 (0.65%)	0 / 143 (0.00%)	0 / 57 (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 adenoma			

subjects affected / exposed	1 / 153 (0.65%)	0 / 143 (0.00%)	0 / 57 (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
Cancer pain			
subjects affected / exposed	1 / 153 (0.65%)	0 / 143 (0.00%)	0 / 57 (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
Tumour associated fever			
subjects affected / exposed	0 / 153 (0.00%)	2 / 143 (1.40%)	0 / 57 (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
Tumour pain			
subjects affected / exposed	0 / 153 (0.00%)	0 / 143 (0.00%)	0 / 57 (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
Vaginal neoplasm			
subjects affected / exposed	1 / 153 (0.65%)	0 / 143 (0.00%)	0 / 57 (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			
Aortic dissection			
subjects affected / exposed	0 / 153 (0.00%)	1 / 143 (0.70%)	0 / 57 (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
Embolism			
subjects affected / exposed	0 / 153 (0.00%)	1 / 143 (0.70%)	0 / 57 (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
Deep vein thrombosis			
subjects affected / exposed	1 / 153 (0.65%)	1 / 143 (0.70%)	0 / 57 (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
Hypertension			

subjects affected / exposed	0 / 153 (0.00%)	1 / 143 (0.70%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Superior vena cava syndrome			
subjects affected / exposed	0 / 153 (0.00%)	1 / 143 (0.70%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	0 / 153 (0.00%)	3 / 143 (2.10%)	0 / 57 (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
Device related thrombosis			
subjects affected / exposed	0 / 153 (0.00%)	1 / 143 (0.70%)	0 / 57 (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
Death			
subjects affected / exposed	1 / 153 (0.65%)	0 / 143 (0.00%)	0 / 57 (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
Chest pain			
subjects affected / exposed	0 / 153 (0.00%)	1 / 143 (0.70%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Asthenia			
subjects affected / exposed	0 / 153 (0.00%)	1 / 143 (0.70%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gait disturbance			
subjects affected / exposed	0 / 153 (0.00%)	1 / 143 (0.70%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General physical health deterioration			

subjects affected / exposed	0 / 153 (0.00%)	1 / 143 (0.70%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mucosal inflammation			
subjects affected / exposed	0 / 153 (0.00%)	0 / 143 (0.00%)	1 / 57 (1.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	4 / 153 (2.61%)	0 / 143 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	2 / 4	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oedema peripheral			
subjects affected / exposed	0 / 153 (0.00%)	1 / 143 (0.70%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 153 (0.00%)	0 / 143 (0.00%)	1 / 57 (1.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cytokine release syndrome			
subjects affected / exposed	0 / 153 (0.00%)	0 / 143 (0.00%)	1 / 57 (1.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Aspiration			
subjects affected / exposed	0 / 153 (0.00%)	1 / 143 (0.70%)	0 / 57 (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
Chronic obstructive pulmonary disease			
subjects affected / exposed	1 / 153 (0.65%)	1 / 143 (0.70%)	0 / 57 (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

Pneumonitis			
subjects affected / exposed	1 / 153 (0.65%)	0 / 143 (0.00%)	1 / 57 (1.75%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Interstitial lung disease			
subjects affected / exposed	0 / 153 (0.00%)	1 / 143 (0.70%)	0 / 57 (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
Hyperventilation			
subjects affected / exposed	0 / 153 (0.00%)	0 / 143 (0.00%)	1 / 57 (1.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	1 / 153 (0.65%)	0 / 143 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	1 / 153 (0.65%)	4 / 143 (2.80%)	1 / 57 (1.75%)
occurrences causally related to treatment / all	0 / 1	1 / 4	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 1
Respiratory failure			
subjects affected / exposed	0 / 153 (0.00%)	0 / 143 (0.00%)	1 / 57 (1.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Psychiatric disorders			
Depression			
subjects affected / exposed	1 / 153 (0.65%)	0 / 143 (0.00%)	0 / 57 (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
Confusional state			
subjects affected / exposed	0 / 153 (0.00%)	1 / 143 (0.70%)	0 / 57 (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
Suicide attempt			

subjects affected / exposed	1 / 153 (0.65%)	0 / 143 (0.00%)	0 / 57 (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			
Liver function test increased			
subjects affected / exposed	0 / 153 (0.00%)	1 / 143 (0.70%)	0 / 57 (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
Neutrophil count decreased			
subjects affected / exposed	0 / 153 (0.00%)	1 / 143 (0.70%)	0 / 57 (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
Norovirus test positive			
subjects affected / exposed	0 / 153 (0.00%)	1 / 143 (0.70%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Accidental overdose			
subjects affected / exposed	1 / 153 (0.65%)	0 / 143 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hip fracture			
subjects affected / exposed	0 / 153 (0.00%)	1 / 143 (0.70%)	0 / 57 (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
Head injury			
subjects affected / exposed	1 / 153 (0.65%)	0 / 143 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal stoma complication			
subjects affected / exposed	0 / 153 (0.00%)	0 / 143 (0.00%)	1 / 57 (1.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Stoma site haemorrhage			
subjects affected / exposed	0 / 153 (0.00%)	1 / 143 (0.70%)	0 / 57 (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
Urinary tract stoma complication			
subjects affected / exposed	0 / 153 (0.00%)	0 / 143 (0.00%)	1 / 57 (1.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tibia fracture			
subjects affected / exposed	1 / 153 (0.65%)	0 / 143 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subdural haematoma			
subjects affected / exposed	1 / 153 (0.65%)	0 / 143 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute coronary syndrome			
subjects affected / exposed	1 / 153 (0.65%)	0 / 143 (0.00%)	0 / 57 (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
Acute myocardial infarction			
subjects affected / exposed	0 / 153 (0.00%)	1 / 143 (0.70%)	0 / 57 (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
Supraventricular tachycardia			
subjects affected / exposed	0 / 153 (0.00%)	1 / 143 (0.70%)	0 / 57 (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
Myocardial infarction			
subjects affected / exposed	1 / 153 (0.65%)	1 / 143 (0.70%)	0 / 57 (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
Cardiac arrest			

subjects affected / exposed	0 / 153 (0.00%)	1 / 143 (0.70%)	0 / 57 (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
Atrial fibrillation			
subjects affected / exposed	1 / 153 (0.65%)	0 / 143 (0.00%)	0 / 57 (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
Angina pectoris			
subjects affected / exposed	1 / 153 (0.65%)	0 / 143 (0.00%)	0 / 57 (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			
Cerebrovascular accident			
subjects affected / exposed	0 / 153 (0.00%)	2 / 143 (1.40%)	0 / 57 (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
Occipital neuralgia			
subjects affected / exposed	1 / 153 (0.65%)	0 / 143 (0.00%)	0 / 57 (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
Aphasia			
subjects affected / exposed	0 / 153 (0.00%)	1 / 143 (0.70%)	0 / 57 (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
Carotid artery stenosis			
subjects affected / exposed	1 / 153 (0.65%)	0 / 143 (0.00%)	0 / 57 (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 infarction			
subjects affected / exposed	1 / 153 (0.65%)	0 / 143 (0.00%)	0 / 57 (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
Amnesia			

subjects affected / exposed	1 / 153 (0.65%)	0 / 143 (0.00%)	0 / 57 (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
Transient ischaemic attack			
subjects affected / exposed	1 / 153 (0.65%)	1 / 143 (0.70%)	0 / 57 (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
Syncope			
subjects affected / exposed	1 / 153 (0.65%)	0 / 143 (0.00%)	0 / 57 (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
Pseudobulbar palsy			
subjects affected / exposed	1 / 153 (0.65%)	0 / 143 (0.00%)	0 / 57 (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
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 153 (0.65%)	2 / 143 (1.40%)	0 / 57 (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
Leukocytosis			
subjects affected / exposed	0 / 153 (0.00%)	1 / 143 (0.70%)	0 / 57 (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
Neutropenia			
subjects affected / exposed	0 / 153 (0.00%)	3 / 143 (2.10%)	0 / 57 (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	1 / 153 (0.65%)	0 / 143 (0.00%)	0 / 57 (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
Febrile neutropenia			

subjects affected / exposed	1 / 153 (0.65%)	6 / 143 (4.20%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 1	5 / 6	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Angle closure glaucoma			
subjects affected / exposed	1 / 153 (0.65%)	0 / 143 (0.00%)	0 / 57 (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
Vision blurred			
subjects affected / exposed	1 / 153 (0.65%)	0 / 143 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	7 / 153 (4.58%)	2 / 143 (1.40%)	2 / 57 (3.51%)
occurrences causally related to treatment / all	0 / 9	1 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Constipation			
subjects affected / exposed	0 / 153 (0.00%)	0 / 143 (0.00%)	1 / 57 (1.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anal fistula			
subjects affected / exposed	0 / 153 (0.00%)	1 / 143 (0.70%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis			
subjects affected / exposed	3 / 153 (1.96%)	0 / 143 (0.00%)	1 / 57 (1.75%)
occurrences causally related to treatment / all	3 / 3	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Autoimmune colitis			
subjects affected / exposed	2 / 153 (1.31%)	0 / 143 (0.00%)	0 / 57 (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
Abdominal pain upper			

subjects affected / exposed	1 / 153 (0.65%)	0 / 143 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enterocolitis			
subjects affected / exposed	0 / 153 (0.00%)	1 / 143 (0.70%)	0 / 57 (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
Duodenal ulcer			
subjects affected / exposed	0 / 153 (0.00%)	0 / 143 (0.00%)	1 / 57 (1.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Duodenal perforation			
subjects affected / exposed	1 / 153 (0.65%)	0 / 143 (0.00%)	0 / 57 (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
Diverticular perforation			
subjects affected / exposed	0 / 153 (0.00%)	1 / 143 (0.70%)	0 / 57 (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
Diarrhoea haemorrhagic			
subjects affected / exposed	1 / 153 (0.65%)	0 / 143 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	4 / 153 (2.61%)	9 / 143 (6.29%)	1 / 57 (1.75%)
occurrences causally related to treatment / all	2 / 4	9 / 9	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Faecaloma			
subjects affected / exposed	0 / 153 (0.00%)	1 / 143 (0.70%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal haemorrhage			

subjects affected / exposed	1 / 153 (0.65%)	1 / 143 (0.70%)	0 / 57 (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
Gastritis			
subjects affected / exposed	1 / 153 (0.65%)	0 / 143 (0.00%)	0 / 57 (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
Intestinal obstruction			
subjects affected / exposed	2 / 153 (1.31%)	2 / 143 (1.40%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Impaired gastric emptying			
subjects affected / exposed	0 / 153 (0.00%)	1 / 143 (0.70%)	0 / 57 (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
Ileus			
subjects affected / exposed	1 / 153 (0.65%)	3 / 143 (2.10%)	1 / 57 (1.75%)
occurrences causally related to treatment / all	1 / 1	1 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal inflammation			
subjects affected / exposed	0 / 153 (0.00%)	1 / 143 (0.70%)	0 / 57 (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
Pancreatitis			
subjects affected / exposed	1 / 153 (0.65%)	0 / 143 (0.00%)	0 / 57 (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
Intra-abdominal haemorrhage			
subjects affected / exposed	0 / 153 (0.00%)	1 / 143 (0.70%)	0 / 57 (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
Large intestinal obstruction			

subjects affected / exposed	1 / 153 (0.65%)	2 / 143 (1.40%)	0 / 57 (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
Large intestine perforation			
subjects affected / exposed	0 / 153 (0.00%)	1 / 143 (0.70%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal perforation			
subjects affected / exposed	0 / 153 (0.00%)	2 / 143 (1.40%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Upper gastrointestinal haemorrhage			
subjects affected / exposed	1 / 153 (0.65%)	1 / 143 (0.70%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Subileus			
subjects affected / exposed	2 / 153 (1.31%)	0 / 143 (0.00%)	0 / 57 (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
Small intestinal obstruction			
subjects affected / exposed	2 / 153 (1.31%)	5 / 143 (3.50%)	3 / 57 (5.26%)
occurrences causally related to treatment / all	0 / 2	0 / 9	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Short-bowel syndrome			
subjects affected / exposed	0 / 153 (0.00%)	1 / 143 (0.70%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	1 / 153 (0.65%)	4 / 143 (2.80%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 1	2 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Autoimmune hepatitis			

subjects affected / exposed	1 / 153 (0.65%)	0 / 143 (0.00%)	0 / 57 (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
Biliary dilatation			
subjects affected / exposed	0 / 153 (0.00%)	1 / 143 (0.70%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute hepatic failure			
subjects affected / exposed	0 / 153 (0.00%)	1 / 143 (0.70%)	0 / 57 (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
Bile duct stenosis			
subjects affected / exposed	0 / 153 (0.00%)	1 / 143 (0.70%)	0 / 57 (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
Cholestasis			
subjects affected / exposed	0 / 153 (0.00%)	1 / 143 (0.70%)	0 / 57 (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
Hepatic failure			
subjects affected / exposed	0 / 153 (0.00%)	0 / 143 (0.00%)	1 / 57 (1.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatitis			
subjects affected / exposed	2 / 153 (1.31%)	0 / 143 (0.00%)	1 / 57 (1.75%)
occurrences causally related to treatment / all	2 / 2	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune-mediated hepatitis			
subjects affected / exposed	1 / 153 (0.65%)	0 / 143 (0.00%)	0 / 57 (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
Cholangitis			

subjects affected / exposed	0 / 153 (0.00%)	2 / 143 (1.40%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Cholangitis acute			
subjects affected / exposed	0 / 153 (0.00%)	0 / 143 (0.00%)	1 / 57 (1.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Cholecystitis			
subjects affected / exposed	0 / 153 (0.00%)	1 / 143 (0.70%)	0 / 57 (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
Cholecystitis acute			
subjects affected / exposed	0 / 153 (0.00%)	1 / 143 (0.70%)	0 / 57 (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
Jaundice cholestatic			
subjects affected / exposed	0 / 153 (0.00%)	1 / 143 (0.70%)	0 / 57 (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 and subcutaneous tissue disorders			
Diabetic foot			
subjects affected / exposed	1 / 153 (0.65%)	1 / 143 (0.70%)	0 / 57 (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
Rash			
subjects affected / exposed	1 / 153 (0.65%)	0 / 143 (0.00%)	0 / 57 (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 erosion			
subjects affected / exposed	0 / 153 (0.00%)	1 / 143 (0.70%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin ulcer			

subjects affected / exposed	0 / 153 (0.00%)	1 / 143 (0.70%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Glomerulonephritis			
subjects affected / exposed	1 / 153 (0.65%)	0 / 143 (0.00%)	0 / 57 (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
Acute kidney injury			
subjects affected / exposed	3 / 153 (1.96%)	2 / 143 (1.40%)	3 / 57 (5.26%)
occurrences causally related to treatment / all	2 / 3	2 / 2	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Autoimmune nephritis			
subjects affected / exposed	0 / 153 (0.00%)	0 / 143 (0.00%)	1 / 57 (1.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal impairment			
subjects affected / exposed	1 / 153 (0.65%)	0 / 143 (0.00%)	0 / 57 (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
Renal failure			
subjects affected / exposed	0 / 153 (0.00%)	1 / 143 (0.70%)	0 / 57 (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
Prerenal failure			
subjects affected / exposed	1 / 153 (0.65%)	0 / 143 (0.00%)	0 / 57 (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
Hydronephrosis			
subjects affected / exposed	1 / 153 (0.65%)	0 / 143 (0.00%)	1 / 57 (1.75%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			

Addison's disease			
subjects affected / exposed	0 / 153 (0.00%)	0 / 143 (0.00%)	1 / 57 (1.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Adrenocortical insufficiency acute			
subjects affected / exposed	1 / 153 (0.65%)	0 / 143 (0.00%)	0 / 57 (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
Adrenal insufficiency			
subjects affected / exposed	2 / 153 (1.31%)	0 / 143 (0.00%)	0 / 57 (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
Autoimmune thyroiditis			
subjects affected / exposed	1 / 153 (0.65%)	0 / 143 (0.00%)	0 / 57 (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			
Pain in jaw			
subjects affected / exposed	0 / 153 (0.00%)	1 / 143 (0.70%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myositis			
subjects affected / exposed	0 / 153 (0.00%)	0 / 143 (0.00%)	1 / 57 (1.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Back pain			
subjects affected / exposed	1 / 153 (0.65%)	0 / 143 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Autoimmune arthritis			
subjects affected / exposed	1 / 153 (0.65%)	0 / 143 (0.00%)	0 / 57 (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

Arthralgia			
subjects affected / exposed	0 / 153 (0.00%)	0 / 143 (0.00%)	1 / 57 (1.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Clostridium difficile colitis			
subjects affected / exposed	0 / 153 (0.00%)	1 / 143 (0.70%)	0 / 57 (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
Cholecystitis infective			
subjects affected / exposed	0 / 153 (0.00%)	1 / 143 (0.70%)	0 / 57 (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
Cellulitis			
subjects affected / exposed	0 / 153 (0.00%)	1 / 143 (0.70%)	0 / 57 (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
COVID-19			
subjects affected / exposed	0 / 153 (0.00%)	0 / 143 (0.00%)	0 / 57 (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
Abdominal sepsis			
subjects affected / exposed	1 / 153 (0.65%)	0 / 143 (0.00%)	0 / 57 (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
Gastrointestinal infection			
subjects affected / exposed	0 / 153 (0.00%)	1 / 143 (0.70%)	0 / 57 (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
Gastroenteritis			
subjects affected / exposed	0 / 153 (0.00%)	1 / 143 (0.70%)	0 / 57 (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
Escherichia sepsis			

subjects affected / exposed	0 / 153 (0.00%)	0 / 143 (0.00%)	1 / 57 (1.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Escherichia pyelonephritis			
subjects affected / exposed	1 / 153 (0.65%)	0 / 143 (0.00%)	0 / 57 (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
Endophthalmitis			
subjects affected / exposed	0 / 153 (0.00%)	0 / 143 (0.00%)	1 / 57 (1.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis			
subjects affected / exposed	1 / 153 (0.65%)	0 / 143 (0.00%)	0 / 57 (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
Device related infection			
subjects affected / exposed	0 / 153 (0.00%)	2 / 143 (1.40%)	1 / 57 (1.75%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infection			
subjects affected / exposed	2 / 153 (1.31%)	0 / 143 (0.00%)	0 / 57 (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
Clostridium difficile infection			
subjects affected / exposed	0 / 153 (0.00%)	1 / 143 (0.70%)	0 / 57 (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
Influenza			
subjects affected / exposed	1 / 153 (0.65%)	2 / 143 (1.40%)	0 / 57 (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
Lower respiratory tract infection			

subjects affected / exposed	0 / 153 (0.00%)	0 / 143 (0.00%)	1 / 57 (1.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymph gland infection			
subjects affected / exposed	0 / 153 (0.00%)	1 / 143 (0.70%)	0 / 57 (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
Meningoencephalitis viral			
subjects affected / exposed	0 / 153 (0.00%)	0 / 143 (0.00%)	1 / 57 (1.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pelvic infection			
subjects affected / exposed	0 / 153 (0.00%)	1 / 143 (0.70%)	0 / 57 (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
Pneumonia			
subjects affected / exposed	3 / 153 (1.96%)	2 / 143 (1.40%)	2 / 57 (3.51%)
occurrences causally related to treatment / all	0 / 3	1 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia streptococcal			
subjects affected / exposed	0 / 153 (0.00%)	1 / 143 (0.70%)	0 / 57 (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
Pyelonephritis			
subjects affected / exposed	1 / 153 (0.65%)	0 / 143 (0.00%)	0 / 57 (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
Pyelonephritis acute			
subjects affected / exposed	0 / 153 (0.00%)	0 / 143 (0.00%)	1 / 57 (1.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stoma site abscess			

subjects affected / exposed	0 / 153 (0.00%)	1 / 143 (0.70%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 153 (0.00%)	1 / 143 (0.70%)	1 / 57 (1.75%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory tract infection			
subjects affected / exposed	0 / 153 (0.00%)	1 / 143 (0.70%)	0 / 57 (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
Stoma site infection			
subjects affected / exposed	1 / 153 (0.65%)	0 / 143 (0.00%)	0 / 57 (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
Urosepsis			
subjects affected / exposed	0 / 153 (0.00%)	2 / 143 (1.40%)	0 / 57 (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
Vascular device infection			
subjects affected / exposed	0 / 153 (0.00%)	0 / 143 (0.00%)	1 / 57 (1.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral infection			
subjects affected / exposed	1 / 153 (0.65%)	0 / 143 (0.00%)	0 / 57 (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	0 / 153 (0.00%)	1 / 143 (0.70%)	1 / 57 (1.75%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Decreased appetite			

subjects affected / exposed	0 / 153 (0.00%)	3 / 143 (2.10%)	0 / 57 (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
Hypoglycaemia			
subjects affected / exposed	0 / 153 (0.00%)	0 / 143 (0.00%)	0 / 57 (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
Hypoalbuminaemia			
subjects affected / exposed	0 / 153 (0.00%)	0 / 143 (0.00%)	1 / 57 (1.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperglycaemia			
subjects affected / exposed	1 / 153 (0.65%)	0 / 143 (0.00%)	0 / 57 (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
Failure to thrive			
subjects affected / exposed	1 / 153 (0.65%)	0 / 143 (0.00%)	0 / 57 (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
Dehydration			
subjects affected / exposed	0 / 153 (0.00%)	4 / 143 (2.80%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 7	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypokalaemia			
subjects affected / exposed	0 / 153 (0.00%)	2 / 143 (1.40%)	0 / 57 (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
Hypomagnesaemia			
subjects affected / exposed	1 / 153 (0.65%)	0 / 143 (0.00%)	0 / 57 (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
Type 2 diabetes mellitus			

subjects affected / exposed	0 / 153 (0.00%)	1 / 143 (0.70%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemia			
subjects affected / exposed	1 / 153 (0.65%)	1 / 143 (0.70%)	1 / 57 (1.75%)
occurrences causally related to treatment / all	1 / 1	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Pembrolizumab Second Course	SOC Crossed over to Pembrolizumab Second Course	
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 12 (25.00%)	1 / 5 (20.00%)	
number of deaths (all causes)	4	2	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder neoplasm			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast cancer			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous cell carcinoma			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal neoplasm			

subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oropharyngeal cancer			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung carcinoma cell type unspecified recurrent			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (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 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colorectal adenoma			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (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 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tumour associated fever			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tumour pain			
subjects affected / exposed	1 / 12 (8.33%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vaginal neoplasm			

subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Aortic dissection			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (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 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Deep vein thrombosis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertension			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Superior vena cava syndrome			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device related thrombosis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (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 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest pain			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Asthenia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (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 / 5 (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 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mucosal inflammation			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (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 / 5 (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 / 5 (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			

Hypersensitivity			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cytokine release syndrome			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (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			
Aspiration			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (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%)	0 / 5 (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 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Interstitial lung disease			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperventilation			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (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 / 5 (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 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (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%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suicide attempt			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Liver function test increased			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutrophil count decreased			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Norovirus test positive			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Injury, poisoning and procedural complications			
Accidental overdose			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hip fracture			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Head injury			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal stoma complication			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stoma site haemorrhage			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract stoma complication			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tibia fracture			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subdural haematoma			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Cardiac disorders			
Acute coronary syndrome			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (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 / 5 (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 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (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 / 5 (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%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina pectoris			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (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			
Cerebrovascular accident			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Occipital neuralgia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aphasia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carotid artery stenosis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral infarction			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Amnesia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (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%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pseudobulbar palsy			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			

Anaemia	subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (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 / 5 (0.00%)	
	occurrences causally related to treatment / all	0 / 0	0 / 0	
	deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenia	subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (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 / 5 (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 / 5 (0.00%)	
	occurrences causally related to treatment / all	0 / 0	0 / 0	
	deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders				
Angle closure glaucoma	subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
	occurrences causally related to treatment / all	0 / 0	0 / 0	
	deaths causally related to treatment / all	0 / 0	0 / 0	
Vision blurred	subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
	occurrences causally related to treatment / all	0 / 0	0 / 0	
	deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders				
Abdominal pain	subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (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 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal fistula			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (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 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Autoimmune colitis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain upper			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterocolitis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenal ulcer			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenal perforation			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticular perforation			

subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea haemorrhagic			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (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%)	0 / 5 (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 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (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%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal obstruction			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Impaired gastric emptying			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileus			

subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal inflammation			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (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 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intra-abdominal haemorrhage			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestinal obstruction			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestine perforation			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal perforation			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper gastrointestinal haemorrhage			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subileus			

subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (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 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Short-bowel syndrome			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (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 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Autoimmune hepatitis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Biliary dilatation			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute hepatic failure			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bile duct stenosis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholestasis			

subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic failure			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune-mediated hepatitis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholangitis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholangitis acute			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis acute			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Jaundice cholestatic			

subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (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			
Diabetic foot			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (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 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin erosion			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin ulcer			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Glomerulonephritis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute kidney injury			
subjects affected / exposed	0 / 12 (0.00%)	1 / 5 (20.00%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Autoimmune nephritis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal impairment			

subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal failure			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prerenal failure			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hydronephrosis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Addison's disease			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adrenocortical insufficiency acute			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adrenal insufficiency			
subjects affected / exposed	1 / 12 (8.33%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Autoimmune thyroiditis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (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			

Pain in jaw			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myositis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (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 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Autoimmune arthritis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthralgia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Clostridium difficile colitis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis infective			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (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 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19			

subjects affected / exposed	1 / 12 (8.33%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal sepsis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal infection			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia sepsis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia pyelonephritis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endophthalmitis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulitis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device related infection			

subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infection			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium difficile infection			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (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 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningoencephalitis viral			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pelvic infection			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			

subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia streptococcal			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis acute			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stoma site abscess			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (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%)	0 / 5 (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 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stoma site infection			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (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 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular device infection			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral infection			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (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 / 5 (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 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoglycaemia			
subjects affected / exposed	1 / 12 (8.33%)	0 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoalbuminaemia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (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 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Failure to thrive			

subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (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 / 5 (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 / 5 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypomagnesaemia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (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 / 5 (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 / 5 (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 First Course	SOC Crossed over to Pembrolizumab
Total subjects affected by non-serious adverse events			
subjects affected / exposed	145 / 153 (94.77%)	142 / 143 (99.30%)	53 / 57 (92.98%)
Vascular disorders			
Hypertension			
subjects affected / exposed	19 / 153 (12.42%)	16 / 143 (11.19%)	2 / 57 (3.51%)
occurrences (all)	25	23	2
Embolism			

subjects affected / exposed	0 / 153 (0.00%)	7 / 143 (4.90%)	0 / 57 (0.00%)
occurrences (all)	0	7	0
Hypotension			
subjects affected / exposed	4 / 153 (2.61%)	3 / 143 (2.10%)	5 / 57 (8.77%)
occurrences (all)	4	3	5
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	19 / 153 (12.42%)	30 / 143 (20.98%)	5 / 57 (8.77%)
occurrences (all)	32	57	8
Oedema peripheral			
subjects affected / exposed	18 / 153 (11.76%)	11 / 143 (7.69%)	10 / 57 (17.54%)
occurrences (all)	24	13	11
Mucosal inflammation			
subjects affected / exposed	7 / 153 (4.58%)	27 / 143 (18.88%)	2 / 57 (3.51%)
occurrences (all)	7	49	2
Malaise			
subjects affected / exposed	10 / 153 (6.54%)	6 / 143 (4.20%)	1 / 57 (1.75%)
occurrences (all)	11	8	1
Influenza like illness			
subjects affected / exposed	14 / 153 (9.15%)	4 / 143 (2.80%)	3 / 57 (5.26%)
occurrences (all)	20	4	3
Impaired healing			
subjects affected / exposed	0 / 153 (0.00%)	1 / 143 (0.70%)	0 / 57 (0.00%)
occurrences (all)	0	1	0
Fatigue			
subjects affected / exposed	58 / 153 (37.91%)	70 / 143 (48.95%)	9 / 57 (15.79%)
occurrences (all)	79	176	9
Chills			
subjects affected / exposed	4 / 153 (2.61%)	7 / 143 (4.90%)	0 / 57 (0.00%)
occurrences (all)	5	9	0
Chest pain			
subjects affected / exposed	8 / 153 (5.23%)	3 / 143 (2.10%)	4 / 57 (7.02%)
occurrences (all)	9	4	5
Pain			

subjects affected / exposed occurrences (all)	4 / 153 (2.61%) 4	3 / 143 (2.10%) 3	0 / 57 (0.00%) 0
Pyrexia subjects affected / exposed occurrences (all)	24 / 153 (15.69%) 29	20 / 143 (13.99%) 28	7 / 57 (12.28%) 9
Temperature intolerance subjects affected / exposed occurrences (all)	1 / 153 (0.65%) 2	8 / 143 (5.59%) 12	0 / 57 (0.00%) 0
Peripheral swelling subjects affected / exposed occurrences (all)	4 / 153 (2.61%) 5	0 / 143 (0.00%) 0	3 / 57 (5.26%) 3
Respiratory, thoracic and mediastinal disorders			
Rhinorrhoea subjects affected / exposed occurrences (all)	9 / 153 (5.88%) 10	13 / 143 (9.09%) 15	1 / 57 (1.75%) 1
Productive cough subjects affected / exposed occurrences (all)	8 / 153 (5.23%) 8	6 / 143 (4.20%) 7	5 / 57 (8.77%) 6
Oropharyngeal pain subjects affected / exposed occurrences (all)	4 / 153 (2.61%) 4	8 / 143 (5.59%) 8	3 / 57 (5.26%) 3
Hiccups subjects affected / exposed occurrences (all)	2 / 153 (1.31%) 3	8 / 143 (5.59%) 10	1 / 57 (1.75%) 1
Epistaxis subjects affected / exposed occurrences (all)	2 / 153 (1.31%) 3	23 / 143 (16.08%) 30	2 / 57 (3.51%) 2
Dyspnoea subjects affected / exposed occurrences (all)	20 / 153 (13.07%) 25	15 / 143 (10.49%) 22	6 / 57 (10.53%) 8
Dysphonia subjects affected / exposed occurrences (all)	2 / 153 (1.31%) 2	8 / 143 (5.59%) 9	0 / 57 (0.00%) 0
Cough			

subjects affected / exposed occurrences (all)	26 / 153 (16.99%) 31	23 / 143 (16.08%) 26	7 / 57 (12.28%) 9
Psychiatric disorders			
Insomnia			
subjects affected / exposed	12 / 153 (7.84%)	10 / 143 (6.99%)	7 / 57 (12.28%)
occurrences (all)	14	11	7
Discouragement			
subjects affected / exposed	0 / 153 (0.00%)	0 / 143 (0.00%)	0 / 57 (0.00%)
occurrences (all)	0	0	0
Depression			
subjects affected / exposed	7 / 153 (4.58%)	5 / 143 (3.50%)	3 / 57 (5.26%)
occurrences (all)	7	5	3
Anxiety			
subjects affected / exposed	9 / 153 (5.88%)	4 / 143 (2.80%)	4 / 57 (7.02%)
occurrences (all)	11	6	4
Anger			
subjects affected / exposed	0 / 153 (0.00%)	0 / 143 (0.00%)	0 / 57 (0.00%)
occurrences (all)	0	0	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	22 / 153 (14.38%)	16 / 143 (11.19%)	5 / 57 (8.77%)
occurrences (all)	33	30	6
Aspartate aminotransferase increased			
subjects affected / exposed	24 / 153 (15.69%)	12 / 143 (8.39%)	6 / 57 (10.53%)
occurrences (all)	33	24	6
Blood alkaline phosphatase increased			
subjects affected / exposed	22 / 153 (14.38%)	6 / 143 (4.20%)	2 / 57 (3.51%)
occurrences (all)	30	9	2
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 153 (0.00%)	0 / 143 (0.00%)	0 / 57 (0.00%)
occurrences (all)	0	0	0
Blood creatinine increased			
subjects affected / exposed	7 / 153 (4.58%)	4 / 143 (2.80%)	2 / 57 (3.51%)
occurrences (all)	8	5	2
Cardiac murmur			

subjects affected / exposed occurrences (all)	1 / 153 (0.65%) 1	1 / 143 (0.70%) 1	1 / 57 (1.75%) 1
Gamma-glutamyltransferase increased subjects affected / exposed occurrences (all)	8 / 153 (5.23%) 8	3 / 143 (2.10%) 5	1 / 57 (1.75%) 2
Neutrophil count decreased subjects affected / exposed occurrences (all)	2 / 153 (1.31%) 2	32 / 143 (22.38%) 65	2 / 57 (3.51%) 10
Platelet count decreased subjects affected / exposed occurrences (all)	2 / 153 (1.31%) 4	10 / 143 (6.99%) 29	2 / 57 (3.51%) 3
Weight decreased subjects affected / exposed occurrences (all)	7 / 153 (4.58%) 7	17 / 143 (11.89%) 17	2 / 57 (3.51%) 2
White blood cell count decreased subjects affected / exposed occurrences (all)	1 / 153 (0.65%) 1	17 / 143 (11.89%) 48	2 / 57 (3.51%) 6
Injury, poisoning and procedural complications Fall subjects affected / exposed occurrences (all)	11 / 153 (7.19%) 13	5 / 143 (3.50%) 5	2 / 57 (3.51%) 2
Cardiac disorders Atrial fibrillation subjects affected / exposed occurrences (all)	3 / 153 (1.96%) 3	2 / 143 (1.40%) 2	0 / 57 (0.00%) 0
Nervous system disorders Peripheral sensory neuropathy subjects affected / exposed occurrences (all)	3 / 153 (1.96%) 3	31 / 143 (21.68%) 51	1 / 57 (1.75%) 1
Dizziness subjects affected / exposed occurrences (all)	24 / 153 (15.69%) 29	27 / 143 (18.88%) 54	6 / 57 (10.53%) 10
Dysgeusia subjects affected / exposed occurrences (all)	5 / 153 (3.27%) 5	13 / 143 (9.09%) 14	0 / 57 (0.00%) 0
Headache			

subjects affected / exposed	21 / 153 (13.73%)	22 / 143 (15.38%)	17 / 57 (29.82%)
occurrences (all)	26	37	27
Hemiparaesthesia			
subjects affected / exposed	0 / 153 (0.00%)	0 / 143 (0.00%)	0 / 57 (0.00%)
occurrences (all)	0	0	0
Hypoaesthesia			
subjects affected / exposed	2 / 153 (1.31%)	5 / 143 (3.50%)	0 / 57 (0.00%)
occurrences (all)	2	7	0
Neuropathy peripheral			
subjects affected / exposed	1 / 153 (0.65%)	28 / 143 (19.58%)	4 / 57 (7.02%)
occurrences (all)	1	41	4
Paraesthesia			
subjects affected / exposed	6 / 153 (3.92%)	8 / 143 (5.59%)	1 / 57 (1.75%)
occurrences (all)	7	10	1
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	1 / 153 (0.65%)	8 / 143 (5.59%)	0 / 57 (0.00%)
occurrences (all)	1	18	0
Anaemia			
subjects affected / exposed	26 / 153 (16.99%)	33 / 143 (23.08%)	9 / 57 (15.79%)
occurrences (all)	32	40	18
Leukopenia			
subjects affected / exposed	0 / 153 (0.00%)	3 / 143 (2.10%)	0 / 57 (0.00%)
occurrences (all)	0	12	0
Lymphadenopathy			
subjects affected / exposed	0 / 153 (0.00%)	0 / 143 (0.00%)	1 / 57 (1.75%)
occurrences (all)	0	0	1
Neutropenia			
subjects affected / exposed	3 / 153 (1.96%)	27 / 143 (18.88%)	0 / 57 (0.00%)
occurrences (all)	4	52	0
Eye disorders			
Vision blurred			
subjects affected / exposed	8 / 153 (5.23%)	2 / 143 (1.40%)	1 / 57 (1.75%)
occurrences (all)	8	2	1
Ocular hyperaemia			

subjects affected / exposed occurrences (all)	5 / 153 (3.27%) 6	0 / 143 (0.00%) 0	1 / 57 (1.75%) 1
Dry eye subjects affected / exposed occurrences (all)	9 / 153 (5.88%) 11	3 / 143 (2.10%) 4	0 / 57 (0.00%) 0
Gastrointestinal disorders			
Abdominal pain upper subjects affected / exposed occurrences (all)	19 / 153 (12.42%) 21	11 / 143 (7.69%) 14	2 / 57 (3.51%) 3
Ascites subjects affected / exposed occurrences (all)	1 / 153 (0.65%) 1	3 / 143 (2.10%) 3	3 / 57 (5.26%) 3
Constipation subjects affected / exposed occurrences (all)	26 / 153 (16.99%) 30	45 / 143 (31.47%) 76	13 / 57 (22.81%) 19
Abdominal pain subjects affected / exposed occurrences (all)	34 / 153 (22.22%) 56	41 / 143 (28.67%) 62	8 / 57 (14.04%) 12
Diarrhoea subjects affected / exposed occurrences (all)	65 / 153 (42.48%) 107	89 / 143 (62.24%) 204	17 / 57 (29.82%) 36
Vomiting subjects affected / exposed occurrences (all)	33 / 153 (21.57%) 53	53 / 143 (37.06%) 85	12 / 57 (21.05%) 20
Stomatitis subjects affected / exposed occurrences (all)	10 / 153 (6.54%) 11	43 / 143 (30.07%) 75	4 / 57 (7.02%) 4
Nausea subjects affected / exposed occurrences (all)	47 / 153 (30.72%) 69	85 / 143 (59.44%) 283	16 / 57 (28.07%) 23
Haemorrhoids subjects affected / exposed occurrences (all)	2 / 153 (1.31%) 2	10 / 143 (6.99%) 10	0 / 57 (0.00%) 0
Gastrooesophageal reflux disease subjects affected / exposed occurrences (all)	5 / 153 (3.27%) 5	6 / 143 (4.20%) 8	1 / 57 (1.75%) 1

Dyspepsia			
subjects affected / exposed	9 / 153 (5.88%)	16 / 143 (11.19%)	5 / 57 (8.77%)
occurrences (all)	10	21	7
Dry mouth			
subjects affected / exposed	17 / 153 (11.11%)	9 / 143 (6.29%)	4 / 57 (7.02%)
occurrences (all)	18	10	5
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	11 / 153 (7.19%)	29 / 143 (20.28%)	0 / 57 (0.00%)
occurrences (all)	11	32	0
Dermatitis acneiform			
subjects affected / exposed	3 / 153 (1.96%)	8 / 143 (5.59%)	1 / 57 (1.75%)
occurrences (all)	6	22	1
Dry skin			
subjects affected / exposed	19 / 153 (12.42%)	14 / 143 (9.79%)	9 / 57 (15.79%)
occurrences (all)	21	15	11
Superficial inflammatory dermatosis			
subjects affected / exposed	0 / 153 (0.00%)	0 / 143 (0.00%)	0 / 57 (0.00%)
occurrences (all)	0	0	0
Rash maculo-papular			
subjects affected / exposed	8 / 153 (5.23%)	3 / 143 (2.10%)	2 / 57 (3.51%)
occurrences (all)	9	3	2
Rash			
subjects affected / exposed	19 / 153 (12.42%)	16 / 143 (11.19%)	10 / 57 (17.54%)
occurrences (all)	27	22	12
Psoriasis			
subjects affected / exposed	4 / 153 (2.61%)	0 / 143 (0.00%)	0 / 57 (0.00%)
occurrences (all)	12	0	0
Pruritus			
subjects affected / exposed	25 / 153 (16.34%)	12 / 143 (8.39%)	15 / 57 (26.32%)
occurrences (all)	37	16	24
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	1 / 153 (0.65%)	25 / 143 (17.48%)	1 / 57 (1.75%)
occurrences (all)	1	35	1
Skin hyperpigmentation			

subjects affected / exposed occurrences (all)	0 / 153 (0.00%) 0	8 / 143 (5.59%) 10	1 / 57 (1.75%) 2
Renal and urinary disorders			
Proteinuria			
subjects affected / exposed	5 / 153 (3.27%)	11 / 143 (7.69%)	2 / 57 (3.51%)
occurrences (all)	7	28	5
Renal impairment			
subjects affected / exposed	1 / 153 (0.65%)	0 / 143 (0.00%)	1 / 57 (1.75%)
occurrences (all)	1	0	1
Endocrine disorders			
Hyperthyroidism			
subjects affected / exposed	6 / 153 (3.92%)	0 / 143 (0.00%)	6 / 57 (10.53%)
occurrences (all)	6	0	6
Hypothyroidism			
subjects affected / exposed	19 / 153 (12.42%)	4 / 143 (2.80%)	7 / 57 (12.28%)
occurrences (all)	20	6	7
Musculoskeletal and connective tissue disorders			
Muscular weakness			
subjects affected / exposed	5 / 153 (3.27%)	1 / 143 (0.70%)	3 / 57 (5.26%)
occurrences (all)	7	1	3
Back pain			
subjects affected / exposed	25 / 153 (16.34%)	24 / 143 (16.78%)	11 / 57 (19.30%)
occurrences (all)	29	27	13
Arthralgia			
subjects affected / exposed	31 / 153 (20.26%)	10 / 143 (6.99%)	12 / 57 (21.05%)
occurrences (all)	52	11	18
Myalgia			
subjects affected / exposed	8 / 153 (5.23%)	12 / 143 (8.39%)	3 / 57 (5.26%)
occurrences (all)	9	15	7
Neck pain			
subjects affected / exposed	4 / 153 (2.61%)	5 / 143 (3.50%)	1 / 57 (1.75%)
occurrences (all)	5	5	1
Pain in extremity			
subjects affected / exposed	18 / 153 (11.76%)	11 / 143 (7.69%)	6 / 57 (10.53%)
occurrences (all)	21	11	7
Muscle spasms			

subjects affected / exposed occurrences (all)	8 / 153 (5.23%) 9	5 / 143 (3.50%) 7	3 / 57 (5.26%) 3
Infections and infestations			
Candida infection			
subjects affected / exposed	1 / 153 (0.65%)	1 / 143 (0.70%)	0 / 57 (0.00%)
occurrences (all)	1	1	0
Cystitis			
subjects affected / exposed	4 / 153 (2.61%)	5 / 143 (3.50%)	4 / 57 (7.02%)
occurrences (all)	4	8	6
Urinary tract infection			
subjects affected / exposed	14 / 153 (9.15%)	15 / 143 (10.49%)	7 / 57 (12.28%)
occurrences (all)	19	23	9
Upper respiratory tract infection			
subjects affected / exposed	16 / 153 (10.46%)	8 / 143 (5.59%)	2 / 57 (3.51%)
occurrences (all)	17	11	2
Tooth infection			
subjects affected / exposed	8 / 153 (5.23%)	5 / 143 (3.50%)	1 / 57 (1.75%)
occurrences (all)	9	5	1
Paronychia			
subjects affected / exposed	1 / 153 (0.65%)	8 / 143 (5.59%)	0 / 57 (0.00%)
occurrences (all)	1	17	0
Oral candidiasis			
subjects affected / exposed	3 / 153 (1.96%)	6 / 143 (4.20%)	4 / 57 (7.02%)
occurrences (all)	4	6	5
Nasopharyngitis			
subjects affected / exposed	20 / 153 (13.07%)	10 / 143 (6.99%)	8 / 57 (14.04%)
occurrences (all)	31	13	12
Influenza			
subjects affected / exposed	7 / 153 (4.58%)	4 / 143 (2.80%)	1 / 57 (1.75%)
occurrences (all)	8	4	1
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	36 / 153 (23.53%)	57 / 143 (39.86%)	2 / 57 (3.51%)
occurrences (all)	49	114	2
Dehydration			

subjects affected / exposed	11 / 153 (7.19%)	7 / 143 (4.90%)	1 / 57 (1.75%)
occurrences (all)	11	7	1
Hypercalcaemia			
subjects affected / exposed	0 / 153 (0.00%)	0 / 143 (0.00%)	2 / 57 (3.51%)
occurrences (all)	0	0	2
Hyperglycaemia			
subjects affected / exposed	8 / 153 (5.23%)	4 / 143 (2.80%)	0 / 57 (0.00%)
occurrences (all)	24	4	0
Hypoalbuminaemia			
subjects affected / exposed	5 / 153 (3.27%)	9 / 143 (6.29%)	0 / 57 (0.00%)
occurrences (all)	5	18	0
Hypokalaemia			
subjects affected / exposed	13 / 153 (8.50%)	23 / 143 (16.08%)	2 / 57 (3.51%)
occurrences (all)	25	38	4
Hyponatraemia			
subjects affected / exposed	10 / 153 (6.54%)	6 / 143 (4.20%)	3 / 57 (5.26%)
occurrences (all)	11	7	4

Non-serious adverse events	Pembrolizumab Second Course	SOC Crossed over to Pembrolizumab Second Course	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	11 / 12 (91.67%)	4 / 5 (80.00%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 12 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Embolism			
subjects affected / exposed	1 / 12 (8.33%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Hypotension			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 12 (8.33%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Oedema peripheral			

subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Mucosal inflammation			
subjects affected / exposed	1 / 12 (8.33%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Malaise			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Influenza like illness			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Impaired healing			
subjects affected / exposed	0 / 12 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Fatigue			
subjects affected / exposed	2 / 12 (16.67%)	0 / 5 (0.00%)	
occurrences (all)	3	0	
Chills			
subjects affected / exposed	0 / 12 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Chest pain			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Pain			
subjects affected / exposed	0 / 12 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Pyrexia			
subjects affected / exposed	0 / 12 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Temperature intolerance			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Peripheral swelling			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Respiratory, thoracic and mediastinal			

disorders			
Rhinorrhoea			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Productive cough			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Oropharyngeal pain			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Hiccups			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Epistaxis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Dyspnoea			
subjects affected / exposed	1 / 12 (8.33%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Dysphonia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Cough			
subjects affected / exposed	1 / 12 (8.33%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Discouragement			
subjects affected / exposed	1 / 12 (8.33%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Depression			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Anxiety			

subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Anger			
subjects affected / exposed	1 / 12 (8.33%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 12 (8.33%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 12 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Blood creatinine increased			
subjects affected / exposed	1 / 12 (8.33%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Cardiac murmur			
subjects affected / exposed	1 / 12 (8.33%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Neutrophil count decreased			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Platelet count decreased			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Weight decreased			

subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 5 (0.00%) 0	
White blood cell count decreased subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 5 (0.00%) 0	
Injury, poisoning and procedural complications Fall subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	1 / 5 (20.00%) 1	
Cardiac disorders Atrial fibrillation subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 5 (0.00%) 0	
Nervous system disorders Peripheral sensory neuropathy subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 5 (0.00%) 0	
Dizziness subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 5 (0.00%) 0	
Dysgeusia subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 5 (0.00%) 0	
Headache subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 5 (0.00%) 0	
Hemiparaesthesia subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	1 / 5 (20.00%) 1	
Hypoaesthesia subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	1 / 5 (20.00%) 1	
Neuropathy peripheral subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 5 (0.00%) 0	
Paraesthesia			

subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 5 (0.00%) 0	
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	0 / 12 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Anaemia			
subjects affected / exposed	1 / 12 (8.33%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Leukopenia			
subjects affected / exposed	0 / 12 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Lymphadenopathy			
subjects affected / exposed	0 / 12 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Neutropenia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Eye disorders			
Vision blurred			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Ocular hyperaemia			
subjects affected / exposed	0 / 12 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Dry eye			
subjects affected / exposed	1 / 12 (8.33%)	0 / 5 (0.00%)	
occurrences (all)	2	0	
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	1 / 12 (8.33%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Ascites			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Constipation			

subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Abdominal pain			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Diarrhoea			
subjects affected / exposed	2 / 12 (16.67%)	0 / 5 (0.00%)	
occurrences (all)	6	0	
Vomiting			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Stomatitis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Nausea			
subjects affected / exposed	1 / 12 (8.33%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Haemorrhoids			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Gastrooesophageal reflux disease			
subjects affected / exposed	2 / 12 (16.67%)	0 / 5 (0.00%)	
occurrences (all)	2	0	
Dyspepsia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Dry mouth			
subjects affected / exposed	1 / 12 (8.33%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Dermatitis acneiform			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	

Dry skin			
subjects affected / exposed	3 / 12 (25.00%)	1 / 5 (20.00%)	
occurrences (all)	3	1	
Superficial inflammatory dermatosis			
subjects affected / exposed	1 / 12 (8.33%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Rash maculo-papular			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Rash			
subjects affected / exposed	2 / 12 (16.67%)	1 / 5 (20.00%)	
occurrences (all)	3	1	
Psoriasis			
subjects affected / exposed	0 / 12 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Pruritus			
subjects affected / exposed	0 / 12 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Palmar-plantar erythrodysesthesia syndrome			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Skin hyperpigmentation			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Renal and urinary disorders			
Proteinuria			
subjects affected / exposed	1 / 12 (8.33%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Renal impairment			
subjects affected / exposed	1 / 12 (8.33%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Endocrine disorders			
Hyperthyroidism			
subjects affected / exposed	1 / 12 (8.33%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Hypothyroidism			

subjects affected / exposed occurrences (all)	2 / 12 (16.67%) 2	0 / 5 (0.00%) 0	
Musculoskeletal and connective tissue disorders			
Muscular weakness			
subjects affected / exposed	1 / 12 (8.33%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Back pain			
subjects affected / exposed	1 / 12 (8.33%)	1 / 5 (20.00%)	
occurrences (all)	1	1	
Arthralgia			
subjects affected / exposed	2 / 12 (16.67%)	0 / 5 (0.00%)	
occurrences (all)	2	0	
Myalgia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Neck pain			
subjects affected / exposed	1 / 12 (8.33%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Pain in extremity			
subjects affected / exposed	1 / 12 (8.33%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Muscle spasms			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Infections and infestations			
Candida infection			
subjects affected / exposed	0 / 12 (0.00%)	1 / 5 (20.00%)	
occurrences (all)	0	1	
Cystitis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Urinary tract infection			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Upper respiratory tract infection			

subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Tooth infection			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Paronychia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Oral candidiasis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Nasopharyngitis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Influenza			
subjects affected / exposed	2 / 12 (16.67%)	0 / 5 (0.00%)	
occurrences (all)	2	0	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 12 (8.33%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Dehydration			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Hypercalcaemia			
subjects affected / exposed	1 / 12 (8.33%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Hyperglycaemia			
subjects affected / exposed	1 / 12 (8.33%)	0 / 5 (0.00%)	
occurrences (all)	1	0	
Hypoalbuminaemia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	
Hypokalaemia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 5 (0.00%)	
occurrences (all)	0	0	

Hyponatraemia			
subjects affected / exposed	1 / 12 (8.33%)	0 / 5 (0.00%)	
occurrences (all)	1	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
08 December 2017	The major changes in the amendment 3 (AM3) included changing overall survival (OS) from a secondary outcome measure to the primary outcome measure, increasing sample size to 300 for interim analysis, changing the time of analyses to allow more data collection for progression-free survival (PFS) and OS outcome measures, allowing standard of care (SOC) participants to resume same therapy after surgery which they were on pre-operatively, allowing drug interruptions after sponsor consultation, and initiating tumor imaging for cross over and second course eligible participants on Cycle 1 Day 1.
15 May 2018	The major changes in the AM4 were to allow for a longer follow-up time, to reflect 35 pembrolizumab treatments in the crossover phase and to allow participants to move from the crossover phase to the second course treatment phase if criteria are met and that timing for final OS analysis was event driven.
14 January 2020	The major change of AM5 included changing the final analysis time for PFS and OS primary outcome measures.
17 May 2021	The major change of AM6 included updating the dose modification and toxicity management guidelines for immune-related adverse events (irAEs).
25 November 2022	The major changes of AM7 included change in the Sponsor entity name and allowing participants to enroll in the pembrolizumab extension study after study completion.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported