Clinical trial results:
A Phase 3, randomized, placebo-controlled, double-blind clinical study of pembrolizumab (MK-3475) with or without lenvatinib (E7080/MK-7902) to evaluate the safety and efficacy of pembrolizumab and lenvatinib as 1L intervention in a PD-L1 selected population of participants with recurrent or metastatic head and neck squamous cell carcinoma (R/M HNSCC) (LEAP-010)

Summary

EudraCT number	2019-003717-34
Trial protocol	ES PL HU DE FR GB IT
Global end of trial date	31 March 2025

Results information

Result version number	v1 (current)
This version publication date	02 April 2026
First version publication date	02 April 2026

Trial information

Trial identification

Sponsor protocol code	7902-010

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04199104
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Merck Sharp & Dohme LLC
Sponsor organisation address	126 East Lincoln Avenue, P.O. Box 2000, Rahway, NJ, United States, 07065
Public contact	Clinical Trials Disclosure, Merck Sharp & Dohme LLC, ClinicalTrialsDisclosure@msd.com
Scientific contact	Clinical Trials Disclosure, Merck Sharp & Dohme LLC, ClinicalTrialsDisclosure@msd.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	31 March 2025
Is this the analysis of the primary completion data?	Yes
Primary completion date	30 May 2023
Global end of trial reached?	Yes
Global end of trial date	31 March 2025
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This is a study of pembrolizumab (MK-3475) with or without lenvatinib (E7080/MK-7902) as a first line intervention in a PD-L1 selected population with participants with recurrent or metastatic head and neck squamous cell carcinoma.
Hypotheses include:
- Pembrolizumab + lenvatinib is superior to pembrolizumab + placebo with respect to Objective Response Rate (ORR) per Response Evaluation Criteria in Solid Tumors Version 1.1 (RECIST 1.1) by blinded independent central review (BICR).
- Pembrolizumab + lenvatinib is superior to pembrolizumab + placebo with respect to Progression Free Survival (PFS) per RECIST 1.1 as assessed by BICR.
- Pembrolizumab + lenvatinib is superior to pembrolizumab + placebo with respect to overall survival (OS).

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	05 February 2020
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	61 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 16
Country: Number of subjects enrolled	Brazil: 34
Country: Number of subjects enrolled	Canada: 12
Country: Number of subjects enrolled	China: 57
Country: Number of subjects enrolled	France: 31
Country: Number of subjects enrolled	Germany: 20
Country: Number of subjects enrolled	Hungary: 24
Country: Number of subjects enrolled	Italy: 19
Country: Number of subjects enrolled	Japan: 47
Country: Number of subjects enrolled	Korea, Republic of: 14
Country: Number of subjects enrolled	Mexico: 19
Country: Number of subjects enrolled	Peru: 26

Country: Number of subjects enrolled	Poland: 24
Country: Number of subjects enrolled	Russian Federation: 20
Country: Number of subjects enrolled	Spain: 14
Country: Number of subjects enrolled	Taiwan: 24
Country: Number of subjects enrolled	Türkiye: 42
Country: Number of subjects enrolled	United Kingdom: 20
Country: Number of subjects enrolled	United States: 48
Worldwide total number of subjects	511
EEA total number of subjects	132

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)	265
From 65 to 84 years	245
85 years and over	1

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Adult participants with recurrent or metastatic head and neck squamous cell carcinoma were enrolled. 511 participants were randomized 1:1 to Arm 1 (Pembrolizumab + Lenvatinib) and Arm 2 (Pembrolizumab + Placebo).

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Pembrolizumab + Lenvatinib

Arm description:

Participants were administered Pembrolizumab 200mg by intravenous (IV) infusion on Day 1 of each 21-day cycle (Q3W) plus Lenvatinib 20 mg orally once a day (QD)

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

Dosage and administration details:

Pembrolizumab 200 mg, every 3 weeks (Q3W) by intravenous (IV) infusion for up to 35 3-week cycles

Investigational medicinal product name	Lenvatinib
Investigational medicinal product code	
Other name	E7080 MK-7902 LENVIMA®
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Lenvatinib, 20 mg (two 10-mg oral capsules) administered once daily (QD)

Arm title	Pembrolizumab + Placebo

Arm description:

Participants were administered Pembrolizumab 200mg by intravenous (IV) infusion on Day 1 of each 21-day cycle (Q3W) plus lenvatinib-matching placebo orally once a day (QD)

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

Dosage and administration details:

Pembrolizumab 200 mg, every 3 weeks (Q3W) by intravenous (IV) infusion for up to 35 3-week cycles

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Lenvatinib-matching placebo, oral capsules, administered QD

Number of subjects in period 1	Pembrolizumab + Lenvatinib	Pembrolizumab + Placebo
Started	256	255
Treated	254	253
Received second course	3	3
Completed	0	0
Not completed	256	255
Consent withdrawn by subject	5	5
Death	182	163
Sponsor Decision	68	85
Lost to follow-up	1	2

Baseline characteristics

Reporting groups	
Reporting group title	Pembrolizumab + Lenvatinib
Reporting group description:	
Participants were administered Pembrolizumab 200mg by intravenous (IV) infusion on Day 1 of each 21-day cycle (Q3W) plus Lenvatinib 20 mg orally once a day (QD)	
Reporting group title	Pembrolizumab + Placebo
Reporting group description:	
Participants were administered Pembrolizumab 200mg by intravenous (IV) infusion on Day 1 of each 21-day cycle (Q3W) plus lenvatinib-matching placebo orally once a day (QD)	

Reporting group values	Pembrolizumab + Lenvatinib	Pembrolizumab + Placebo	Total
Number of subjects	256	255	511
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	124	141	265
From 65-84 years	132	113	245
85 years and over	0	1	1
Age Continuous Units: Years			
arithmetic mean	64.0	62.7	
standard deviation	± 8.8	± 9.6	-
Sex: Female, Male Units:			
Female	37	42	79
Male	219	213	432
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	2	7	9
Asian	67	80	147
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	2	2	4
White	168	147	315
More than one race	17	19	36
Unknown or Not Reported	0	0	0
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	33	42	75
Not Hispanic or Latino	205	199	404
Unknown or Not Reported	18	14	32

Programmed Cell Death Ligand 1 (PD-L1) Tumor Expression			
Participants were assessed for their PD- L1 tumor expression level by immunohistochemistry assay using tumor tissue from a newly obtained biopsy. PD-L1 expression analyses were restricted to only tumor cells with TPS (tumor proportion scoring) <50% vs ≥50%.			
Units: Subjects			
<50%	192	191	383
>=50%	64	64	128
Human Papilloma Virus (HPV) Status			
HPV status for oropharynx cancer as determined by immunohistochemistry (positive or negative); HPV status for participants without oropharynx cancer (eg, cancers of the oral cavity, hypopharynx and larynx) is considered HPV negative.			
Units: Subjects			
Positive	57	58	115
Negative	199	197	396
Eastern Cooperative Oncology Group (ECOG Status of 0 vs 1)			
Participants were stratified on basis of their ECOG status of 0 vs 1. The ECOG status 0 meant fully active, able to carry on all pre-disease performance without restriction, whereas an ECOG status 1 meant restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature.			
Units: Subjects			
ECOG 0	122	115	237
ECOG 1	134	140	274

End points

End points reporting groups

Reporting group title	Pembrolizumab + Lenvatinib
Reporting group description:	
Participants were administered Pembrolizumab 200mg by intravenous (IV) infusion on Day 1 of each 21-day cycle (Q3W) plus Lenvatinib 20 mg orally once a day (QD)	
Reporting group title	Pembrolizumab + Placebo
Reporting group description:	
Participants were administered Pembrolizumab 200mg by intravenous (IV) infusion on Day 1 of each 21-day cycle (Q3W) plus lenvatinib-matching placebo orally once a day (QD)	

Primary: Objective Response Rate (ORR) per Response Evaluation Criteria in Solid Tumors Version 1.1 (RECIST 1.1) as Assessed by Blinded Independent Central Review (BICR)

End point title	Objective Response Rate (ORR) per Response Evaluation Criteria in Solid Tumors Version 1.1 (RECIST 1.1) as Assessed by Blinded Independent Central Review (BICR)
End point description:	
ORR is defined as the percentage of participants who had 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, taking as reference the baseline sum diameters) per RECIST 1.1 modified to follow a maximum of 10 target lesions and a maximum of 5 target lesions per organ. The percentage of participants who experienced a CR or PR based on modified RECIST 1.1 is presented. Participants were included in the treatment group to which they were randomized.	
End point type	Primary
End point timeframe:	
Up to ~ 37 months	

End point values	Pembrolizumab + Lenvatinib	Pembrolizumab + Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	256	255		
Units: Percentage of participants				
number (confidence interval 95%)	46.9 (40.6 to 53.2)	27.5 (22.1 to 33.4)		

Statistical analyses

Statistical analysis title	Point Estimate of Objective Response Rate
Comparison groups	Pembrolizumab + Lenvatinib v Pembrolizumab + Placebo

Number of subjects included in analysis	511
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0000019
Method	Miettinen and Nurminen method
Parameter estimate	point estimate
Point estimate	19.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	11.2
upper limit	27.3

Primary: Progression Free Survival (PFS) per Response Evaluation Criteria in Solid Tumors Version 1.1 (RECIST 1.1) as Assessed by Blinded Independent Central Review (BICR).

End point title	Progression Free Survival (PFS) per Response Evaluation Criteria in Solid Tumors Version 1.1 (RECIST 1.1) as Assessed by Blinded Independent Central Review (BICR).

End point description:

PFS is defined as the time from randomization to the first documented progressive disease (PD) or death due to any cause, whichever occurs first. Per RECIST 1.1, PD was defined as ≥20% increase in the sum of diameters of target lesions. In addition to the relative increase of 20%, the sum must also demonstrate an absolute increase of ≥5 mm. Note: The appearance of one or more new lesions is also considered PD. Participants were included in the treatment group to which they were randomized.

End point type	Primary

End point timeframe:

Up to ~ 37 months

End point values	Pembrolizumab + Lenvatinib	Pembrolizumab + Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	256	255		
Units: Months				
median (confidence interval 95%)	7.0 (5.6 to 8.0)	2.8 (2.6 to 4.1)		

Statistical analyses

Statistical analysis title	Hazard Ratio of Progression Free Survival
Comparison groups	Pembrolizumab + Lenvatinib v Pembrolizumab + Placebo

Number of subjects included in analysis	511
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0001129
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.68
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.55
upper limit	0.83

Primary: Overall Survival (OS)	
End point title	Overall Survival (OS)
End point description:	
OS is the time from randomization to death due to any cause. Participants were included in the treatment group to which they were randomized.	
End point type	Primary
End point timeframe:	
Up to ~ 37 months	

End point values	Pembrolizumab + Lenvatinib	Pembrolizumab + Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	256	255		
Units: Months				
median (confidence interval 95%)	15.0 (13.2 to 17.0)	17.9 (13.8 to 21.6)		

Statistical analyses

Statistical analysis title	Hazard Ratio of Overall Survival
Comparison groups	Pembrolizumab + Lenvatinib v Pembrolizumab + Placebo
Number of subjects included in analysis	511
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8819584
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	1.15

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.91
upper limit	1.45

Secondary: Duration of Response (DOR)

End point title	Duration of Response (DOR)

End point description:

For all randomized participants who demonstrate a confirmed complete response (CR: Disappearance of all target lesions) or confirmed Partial Response (PR: At least a 30% decrease in the sum of diameters of target lesions) per RECIST 1.1, DOR is defined as the time from first documented evidence of CR or PR until disease progression or death. Participants were included in the treatment group to which they were randomized. A value of 9999 indicates the endpoint was not reached.

End point type	Secondary

End point timeframe:

Up to ~ 37 months

End point values	Pembrolizumab + Lenvatinib	Pembrolizumab + Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	120	70		
Units: Months				
median (confidence interval 95%)	10.1 (8.3 to 13.9)	9999 (11.9 to 9999)		

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

An adverse event (AE) is defined as any unfavorable and unintended sign including an abnormal laboratory finding, symptom or disease associated with the use of a medical treatment or procedure, regardless of whether it is considered related to the medical treatment or procedure, that occurs during the course of the study. Safety analyses were conducted in the all-participants-as-treated (APaT) population, which consisted of all randomized participants who received at least one dose of study treatment. Participants were included in the treatment group corresponding to the study treatment they actually received.

End point type	Secondary

End point timeframe:

Up to ~ 61 months

End point values	Pembrolizumab + Lenvatinib	Pembrolizumab + Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	254	253		
Units: Percentage of Participants				
number (not applicable)	99.21	96.84		

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

An adverse event (AE) is defined as any unfavorable and unintended sign including an abnormal laboratory finding, symptom or disease associated with the use of a medical treatment or procedure, regardless of whether it is considered related to the medical treatment or procedure, that occurs during the course of the study. Safety analyses were conducted in the APaT population, which consisted of all randomized participants who received at least one dose of study treatment. Participants were included in the treatment group corresponding to the study treatment they actually received.

End point type	Secondary

End point timeframe:

Up to ~ 46 months

End point values	Pembrolizumab + Lenvatinib	Pembrolizumab + Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	254	253		
Units: Percentage of Participants				
number (not applicable)	46.9	15.8		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to ~ 61 months

Adverse event reporting additional description:

All-cause mortality includes all randomized participants (n=511). Adverse events (AEs) include all randomized participants who received ≥1 dose of study drug. Cancer disease progression was not an AE unless study related. MedDRA terms neoplasm progression, malignant neoplasm progression & disease progression unrelated to study drug were excluded.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	28.0

Reporting groups

Reporting group title	Pembrolizumab + Lenvatinib (First Course)
Reporting group description: -	
Reporting group title	Pembrolizumab + Placebo (Second Course)
Reporting group description: -	
Reporting group title	Pembrolizumab + Lenvatinib (Second Course)
Reporting group description: -	
Reporting group title	Pembrolizumab + Placebo (First Course)

Reporting group description: -

Serious adverse events	Pembrolizumab + Lenvatinib (First Course)	Pembrolizumab + Placebo (Second Course)	Pembrolizumab + Lenvatinib (Second Course)
Total subjects affected by serious adverse events			
subjects affected / exposed	155 / 254 (61.02%)	2 / 3 (66.67%)	1 / 3 (33.33%)
number of deaths (all causes)	185	0	1
number of deaths resulting from adverse events	41	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Oral haemangioma			
subjects affected / exposed	0 / 254 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Leiomyoma			
subjects affected / exposed	0 / 254 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infected neoplasm			

subjects affected / exposed	2 / 254 (0.79%)	0 / 3 (0.00%)	0 / 3 (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
Bladder transitional cell carcinoma stage 0			
subjects affected / exposed	0 / 254 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Basal cell carcinoma			
subjects affected / exposed	1 / 254 (0.39%)	0 / 3 (0.00%)	0 / 3 (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
Oropharyngeal squamous cell carcinoma			
subjects affected / exposed	0 / 254 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Squamous cell carcinoma of skin			
subjects affected / exposed	0 / 254 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tumour pain			
subjects affected / exposed	2 / 254 (0.79%)	0 / 3 (0.00%)	0 / 3 (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
Tumour haemorrhage			
subjects affected / exposed	10 / 254 (3.94%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	11 / 14	0 / 0	0 / 0
deaths causally related to treatment / all	3 / 5	0 / 0	0 / 0
Vascular disorders			
Arterial haemorrhage			
subjects affected / exposed	1 / 254 (0.39%)	0 / 3 (0.00%)	0 / 3 (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
Embolism			

subjects affected / exposed	2 / 254 (0.79%)	0 / 3 (0.00%)	0 / 3 (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
Hypertension			
subjects affected / exposed	3 / 254 (1.18%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	1 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypotension			
subjects affected / exposed	3 / 254 (1.18%)	0 / 3 (0.00%)	0 / 3 (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
Orthostatic hypotension			
subjects affected / exposed	1 / 254 (0.39%)	0 / 3 (0.00%)	0 / 3 (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
Vascular occlusion			
subjects affected / exposed	0 / 254 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral arterial occlusive disease			
subjects affected / exposed	1 / 254 (0.39%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 254 (0.39%)	0 / 3 (0.00%)	0 / 3 (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
Death			
subjects affected / exposed	6 / 254 (2.36%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 6	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 6	0 / 0	0 / 0
Pyrexia			

subjects affected / exposed	3 / 254 (1.18%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	1 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General physical health deterioration			
subjects affected / exposed	2 / 254 (0.79%)	0 / 3 (0.00%)	0 / 3 (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
Malaise			
subjects affected / exposed	1 / 254 (0.39%)	0 / 3 (0.00%)	0 / 3 (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
Mucosal inflammation			
subjects affected / exposed	1 / 254 (0.39%)	0 / 3 (0.00%)	0 / 3 (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
Pain			
subjects affected / exposed	0 / 254 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fatigue			
subjects affected / exposed	2 / 254 (0.79%)	0 / 3 (0.00%)	0 / 3 (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
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 254 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Prostatitis			
subjects affected / exposed	0 / 254 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Respiratory, thoracic and mediastinal disorders			
Aspiration			
subjects affected / exposed	2 / 254 (0.79%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 2	0 / 0	0 / 0
Apnoea			
subjects affected / exposed	0 / 254 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute respiratory failure			
subjects affected / exposed	0 / 254 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute respiratory distress syndrome			
subjects affected / exposed	0 / 254 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Acquired tracheo-oesophageal fistula			
subjects affected / exposed	0 / 254 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Laryngeal stenosis			
subjects affected / exposed	2 / 254 (0.79%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune-mediated lung disease			
subjects affected / exposed	1 / 254 (0.39%)	0 / 3 (0.00%)	0 / 3 (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
Haemoptysis			
subjects affected / exposed	2 / 254 (0.79%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Epistaxis			
subjects affected / exposed	3 / 254 (1.18%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	1 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Autoimmune lung disease			
subjects affected / exposed	0 / 254 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Chronic obstructive pulmonary disease			
subjects affected / exposed	2 / 254 (0.79%)	0 / 3 (0.00%)	0 / 3 (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
Bronchopleural fistula			
subjects affected / exposed	1 / 254 (0.39%)	0 / 3 (0.00%)	0 / 3 (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
Bronchial obstruction			
subjects affected / exposed	1 / 254 (0.39%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	5 / 254 (1.97%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	1 / 5	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Oropharyngeal fistula			
subjects affected / exposed	1 / 254 (0.39%)	0 / 3 (0.00%)	0 / 3 (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
Oropharyngeal pain			
subjects affected / exposed	2 / 254 (0.79%)	0 / 3 (0.00%)	0 / 3 (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
Pharyngeal haemorrhage			

subjects affected / exposed	2 / 254 (0.79%)	0 / 3 (0.00%)	0 / 3 (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
Pleural effusion			
subjects affected / exposed	1 / 254 (0.39%)	0 / 3 (0.00%)	0 / 3 (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
Pleurisy			
subjects affected / exposed	0 / 254 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Pneumomediastinum			
subjects affected / exposed	0 / 254 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonitis			
subjects affected / exposed	3 / 254 (1.18%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	2 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumothorax			
subjects affected / exposed	2 / 254 (0.79%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	1 / 254 (0.39%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Obstructive airways disorder			
subjects affected / exposed	0 / 254 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary haemorrhage			

subjects affected / exposed	1 / 254 (0.39%)	0 / 3 (0.00%)	0 / 3 (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
Respiratory failure			
subjects affected / exposed	3 / 254 (1.18%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Tracheal fistula			
subjects affected / exposed	2 / 254 (0.79%)	0 / 3 (0.00%)	0 / 3 (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
Psychiatric disorders			
Delirium			
subjects affected / exposed	2 / 254 (0.79%)	0 / 3 (0.00%)	0 / 3 (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
Alcohol withdrawal syndrome			
subjects affected / exposed	0 / 254 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Confusional state			
subjects affected / exposed	0 / 254 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Product issues			
Device occlusion			
subjects affected / exposed	1 / 254 (0.39%)	0 / 3 (0.00%)	0 / 3 (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 dislocation			
subjects affected / exposed	4 / 254 (1.57%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			

Weight decreased			
subjects affected / exposed	2 / 254 (0.79%)	0 / 3 (0.00%)	0 / 3 (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
Platelet count decreased			
subjects affected / exposed	2 / 254 (0.79%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood urea increased			
subjects affected / exposed	1 / 254 (0.39%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Concussion			
subjects affected / exposed	1 / 254 (0.39%)	0 / 3 (0.00%)	0 / 3 (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
Post procedural haemorrhage			
subjects affected / exposed	2 / 254 (0.79%)	0 / 3 (0.00%)	0 / 3 (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
Osteoradionecrosis			
subjects affected / exposed	1 / 254 (0.39%)	0 / 3 (0.00%)	0 / 3 (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
Humerus fracture			
subjects affected / exposed	1 / 254 (0.39%)	0 / 3 (0.00%)	0 / 3 (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
Head injury			
subjects affected / exposed	1 / 254 (0.39%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Tracheal obstruction			
subjects affected / exposed	0 / 254 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Fibula fracture			
subjects affected / exposed	0 / 254 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Contusion			
subjects affected / exposed	1 / 254 (0.39%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Radiation necrosis			
subjects affected / exposed	0 / 254 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Stoma site haemorrhage			
subjects affected / exposed	2 / 254 (0.79%)	0 / 3 (0.00%)	0 / 3 (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
Gastrostomy tube site complication			
subjects affected / exposed	0 / 254 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound complication			
subjects affected / exposed	1 / 254 (0.39%)	0 / 3 (0.00%)	0 / 3 (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 pseudoaneurysm			
subjects affected / exposed	1 / 254 (0.39%)	0 / 3 (0.00%)	0 / 3 (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
Congenital, familial and genetic disorders			

Tracheo-oesophageal fistula			
subjects affected / exposed	0 / 254 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Bradyarrhythmia			
subjects affected / exposed	0 / 254 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute myocardial infarction			
subjects affected / exposed	4 / 254 (1.57%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 2	0 / 0	0 / 0
Atrial fibrillation			
subjects affected / exposed	1 / 254 (0.39%)	0 / 3 (0.00%)	0 / 3 (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 left ventricular failure			
subjects affected / exposed	0 / 254 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac arrest			
subjects affected / exposed	2 / 254 (0.79%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 2	0 / 0	0 / 0
Cardiac failure			
subjects affected / exposed	2 / 254 (0.79%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Cardiovascular disorder			
subjects affected / exposed	1 / 254 (0.39%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Cardiac tamponade			

subjects affected / exposed	1 / 254 (0.39%)	0 / 3 (0.00%)	0 / 3 (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
Cardiomyopathy			
subjects affected / exposed	1 / 254 (0.39%)	0 / 3 (0.00%)	0 / 3 (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
Cardiac failure acute			
subjects affected / exposed	1 / 254 (0.39%)	0 / 3 (0.00%)	0 / 3 (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
Cardiovascular insufficiency			
subjects affected / exposed	0 / 254 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Coronary artery stenosis			
subjects affected / exposed	0 / 254 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	1 / 254 (0.39%)	0 / 3 (0.00%)	0 / 3 (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
Sinus node dysfunction			
subjects affected / exposed	1 / 254 (0.39%)	0 / 3 (0.00%)	0 / 3 (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
Palpitations			
subjects affected / exposed	1 / 254 (0.39%)	0 / 3 (0.00%)	0 / 3 (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
Pericardial effusion			

subjects affected / exposed	1 / 254 (0.39%)	0 / 3 (0.00%)	0 / 3 (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
Myocarditis			
subjects affected / exposed	1 / 254 (0.39%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Cerebral infarction			
subjects affected / exposed	0 / 254 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Cerebral haemorrhage			
subjects affected / exposed	1 / 254 (0.39%)	0 / 3 (0.00%)	0 / 3 (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
Autonomic dysreflexia			
subjects affected / exposed	1 / 254 (0.39%)	0 / 3 (0.00%)	0 / 3 (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 ischaemia			
subjects affected / exposed	1 / 254 (0.39%)	0 / 3 (0.00%)	0 / 3 (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
Headache			
subjects affected / exposed	2 / 254 (0.79%)	0 / 3 (0.00%)	0 / 3 (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
Haemorrhagic stroke			
subjects affected / exposed	1 / 254 (0.39%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetic hyperosmolar coma			

subjects affected / exposed	0 / 254 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrovascular accident			
subjects affected / exposed	2 / 254 (0.79%)	0 / 3 (0.00%)	0 / 3 (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
Ischaemic stroke			
subjects affected / exposed	1 / 254 (0.39%)	0 / 3 (0.00%)	0 / 3 (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
Peripheral sensorimotor neuropathy			
subjects affected / exposed	1 / 254 (0.39%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal cord compression			
subjects affected / exposed	1 / 254 (0.39%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 254 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	3 / 254 (1.18%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	2 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile bone marrow aplasia			
subjects affected / exposed	1 / 254 (0.39%)	0 / 3 (0.00%)	0 / 3 (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
Ear and labyrinth disorders			

Vertigo			
subjects affected / exposed	2 / 254 (0.79%)	0 / 3 (0.00%)	0 / 3 (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
Gastrointestinal disorders			
Colitis			
subjects affected / exposed	1 / 254 (0.39%)	0 / 3 (0.00%)	0 / 3 (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
Abdominal pain			
subjects affected / exposed	2 / 254 (0.79%)	0 / 3 (0.00%)	0 / 3 (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
Constipation			
subjects affected / exposed	0 / 254 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Diarrhoea			
subjects affected / exposed	5 / 254 (1.97%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	4 / 5	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dysphagia			
subjects affected / exposed	7 / 254 (2.76%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	3 / 8	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enteritis			
subjects affected / exposed	1 / 254 (0.39%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune-mediated enterocolitis			
subjects affected / exposed	1 / 254 (0.39%)	0 / 3 (0.00%)	0 / 3 (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
Gastric haemorrhage			

subjects affected / exposed	1 / 254 (0.39%)	0 / 3 (0.00%)	0 / 3 (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
Gastric ulcer			
subjects affected / exposed	1 / 254 (0.39%)	0 / 3 (0.00%)	0 / 3 (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 haemorrhage			
subjects affected / exposed	1 / 254 (0.39%)	0 / 3 (0.00%)	0 / 3 (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
Haematemesis			
subjects affected / exposed	0 / 254 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enterocolitis			
subjects affected / exposed	1 / 254 (0.39%)	0 / 3 (0.00%)	0 / 3 (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	1 / 254 (0.39%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestine perforation			
subjects affected / exposed	2 / 254 (0.79%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Lower gastrointestinal haemorrhage			
subjects affected / exposed	1 / 254 (0.39%)	0 / 3 (0.00%)	0 / 3 (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
Oesophageal stenosis			

subjects affected / exposed	1 / 254 (0.39%)	0 / 3 (0.00%)	0 / 3 (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
Mouth haemorrhage			
subjects affected / exposed	3 / 254 (1.18%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	1 / 254 (0.39%)	0 / 3 (0.00%)	0 / 3 (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
Melaena			
subjects affected / exposed	1 / 254 (0.39%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophagitis			
subjects affected / exposed	1 / 254 (0.39%)	0 / 3 (0.00%)	0 / 3 (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
Oral pain			
subjects affected / exposed	0 / 254 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Pancreatic mass			
subjects affected / exposed	0 / 254 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Stomatitis			
subjects affected / exposed	2 / 254 (0.79%)	0 / 3 (0.00%)	0 / 3 (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
Pancreatitis acute			

subjects affected / exposed	1 / 254 (0.39%)	0 / 3 (0.00%)	0 / 3 (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
Salivary duct inflammation			
subjects affected / exposed	1 / 254 (0.39%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal obstruction			
subjects affected / exposed	1 / 254 (0.39%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis			
subjects affected / exposed	0 / 254 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper gastrointestinal haemorrhage			
subjects affected / exposed	3 / 254 (1.18%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	2 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	2 / 3	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	4 / 254 (1.57%)	0 / 3 (0.00%)	0 / 3 (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
Hepatobiliary disorders			
Cholangitis			
subjects affected / exposed	1 / 254 (0.39%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholangitis acute			
subjects affected / exposed	1 / 254 (0.39%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis			

subjects affected / exposed	1 / 254 (0.39%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis acute			
subjects affected / exposed	2 / 254 (0.79%)	0 / 3 (0.00%)	0 / 3 (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
Hepatitis			
subjects affected / exposed	1 / 254 (0.39%)	0 / 3 (0.00%)	0 / 3 (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
Hypertransaminasaemia			
subjects affected / exposed	1 / 254 (0.39%)	0 / 3 (0.00%)	0 / 3 (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
Liver injury			
subjects affected / exposed	1 / 254 (0.39%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic failure			
subjects affected / exposed	0 / 254 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Dermatitis			
subjects affected / exposed	1 / 254 (0.39%)	0 / 3 (0.00%)	0 / 3 (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
Drug eruption			
subjects affected / exposed	1 / 254 (0.39%)	0 / 3 (0.00%)	0 / 3 (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 ulcer			

subjects affected / exposed	1 / 254 (0.39%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Nephrotic syndrome			
subjects affected / exposed	1 / 254 (0.39%)	0 / 3 (0.00%)	0 / 3 (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
Urinary retention			
subjects affected / exposed	0 / 254 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal impairment			
subjects affected / exposed	1 / 254 (0.39%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
Adrenal insufficiency			
subjects affected / exposed	2 / 254 (0.79%)	0 / 3 (0.00%)	0 / 3 (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
Hypercalcaemia of malignancy			
subjects affected / exposed	0 / 254 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypopituitarism			
subjects affected / exposed	0 / 254 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Hypothyroidism			
subjects affected / exposed	1 / 254 (0.39%)	0 / 3 (0.00%)	0 / 3 (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
Inappropriate antidiuretic hormone			

secretion			
subjects affected / exposed	1 / 254 (0.39%)	0 / 3 (0.00%)	0 / 3 (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
Hyperthyroidism			
subjects affected / exposed	1 / 254 (0.39%)	0 / 3 (0.00%)	0 / 3 (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			
Arthritis			
subjects affected / exposed	0 / 254 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Soft tissue swelling			
subjects affected / exposed	0 / 254 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Scleroderma			
subjects affected / exposed	0 / 254 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Osteonecrosis of jaw			
subjects affected / exposed	3 / 254 (1.18%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	2 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neck pain			
subjects affected / exposed	1 / 254 (0.39%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematoma muscle			
subjects affected / exposed	0 / 254 (0.00%)	0 / 3 (0.00%)	0 / 3 (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

Flank pain			
subjects affected / exposed	0 / 254 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Fistula			
subjects affected / exposed	1 / 254 (0.39%)	0 / 3 (0.00%)	0 / 3 (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
Trismus			
subjects affected / exposed	1 / 254 (0.39%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Abdominal abscess			
subjects affected / exposed	1 / 254 (0.39%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal infection			
subjects affected / exposed	1 / 254 (0.39%)	0 / 3 (0.00%)	0 / 3 (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
Abscess neck			
subjects affected / exposed	2 / 254 (0.79%)	0 / 3 (0.00%)	0 / 3 (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
Anal abscess			
subjects affected / exposed	1 / 254 (0.39%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis			
subjects affected / exposed	1 / 254 (0.39%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			

subjects affected / exposed	0 / 254 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	1 / 254 (0.39%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19			
subjects affected / exposed	3 / 254 (1.18%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 2	0 / 0	0 / 0
COVID-19 pneumonia			
subjects affected / exposed	1 / 254 (0.39%)	0 / 3 (0.00%)	0 / 3 (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
Catheter site infection			
subjects affected / exposed	1 / 254 (0.39%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis perforated			
subjects affected / exposed	1 / 254 (0.39%)	0 / 3 (0.00%)	0 / 3 (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
Cystitis			
subjects affected / exposed	0 / 254 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Empyema			
subjects affected / exposed	1 / 254 (0.39%)	0 / 3 (0.00%)	0 / 3 (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
Fournier's gangrene			

subjects affected / exposed	1 / 254 (0.39%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	1 / 254 (0.39%)	0 / 3 (0.00%)	0 / 3 (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
Perirectal abscess			
subjects affected / exposed	1 / 254 (0.39%)	0 / 3 (0.00%)	0 / 3 (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
Lung abscess			
subjects affected / exposed	1 / 254 (0.39%)	0 / 3 (0.00%)	0 / 3 (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
Necrotising soft tissue infection			
subjects affected / exposed	1 / 254 (0.39%)	0 / 3 (0.00%)	0 / 3 (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
Perineal abscess			
subjects affected / exposed	1 / 254 (0.39%)	0 / 3 (0.00%)	0 / 3 (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
Infected skin ulcer			
subjects affected / exposed	1 / 254 (0.39%)	0 / 3 (0.00%)	0 / 3 (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
Pharyngitis			
subjects affected / exposed	1 / 254 (0.39%)	0 / 3 (0.00%)	0 / 3 (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
Pneumococcal infection			

subjects affected / exposed	1 / 254 (0.39%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	21 / 254 (8.27%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	5 / 25	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 4	0 / 0	0 / 0
Pneumonia acinetobacter			
subjects affected / exposed	1 / 254 (0.39%)	0 / 3 (0.00%)	0 / 3 (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
Rectal abscess			
subjects affected / exposed	1 / 254 (0.39%)	0 / 3 (0.00%)	0 / 3 (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
Pneumonia bacterial			
subjects affected / exposed	2 / 254 (0.79%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia necrotising			
subjects affected / exposed	1 / 254 (0.39%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia viral			
subjects affected / exposed	1 / 254 (0.39%)	0 / 3 (0.00%)	0 / 3 (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
Rash pustular			
subjects affected / exposed	0 / 254 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia aspiration			

subjects affected / exposed	7 / 254 (2.76%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	2 / 8	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 2	0 / 0	0 / 0
Respiratory tract infection			
subjects affected / exposed	1 / 254 (0.39%)	0 / 3 (0.00%)	0 / 3 (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
Sepsis			
subjects affected / exposed	2 / 254 (0.79%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Skin infection			
subjects affected / exposed	1 / 254 (0.39%)	0 / 3 (0.00%)	0 / 3 (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
Stoma site infection			
subjects affected / exposed	2 / 254 (0.79%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 5	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tracheitis			
subjects affected / exposed	1 / 254 (0.39%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	3 / 254 (1.18%)	0 / 3 (0.00%)	0 / 3 (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
Urinary tract infection			
subjects affected / exposed	2 / 254 (0.79%)	0 / 3 (0.00%)	0 / 3 (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
Urosepsis			

subjects affected / exposed	0 / 254 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	5 / 254 (1.97%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	3 / 5	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Decreased appetite			
subjects affected / exposed	4 / 254 (1.57%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	6 / 6	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetic ketoacidosis			
subjects affected / exposed	0 / 254 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Fulminant type 1 diabetes mellitus			
subjects affected / exposed	1 / 254 (0.39%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypercalcaemia			
subjects affected / exposed	3 / 254 (1.18%)	0 / 3 (0.00%)	0 / 3 (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
Hyperglycaemia			
subjects affected / exposed	1 / 254 (0.39%)	0 / 3 (0.00%)	0 / 3 (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
Type 2 diabetes mellitus			
subjects affected / exposed	0 / 254 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Malnutrition			

subjects affected / exposed	2 / 254 (0.79%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	1 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemia			
subjects affected / exposed	2 / 254 (0.79%)	0 / 3 (0.00%)	0 / 3 (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
Hypokalaemia			
subjects affected / exposed	0 / 254 (0.00%)	0 / 3 (0.00%)	0 / 3 (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	2 / 254 (0.79%)	0 / 3 (0.00%)	0 / 3 (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
Hyperkalaemia			
subjects affected / exposed	0 / 254 (0.00%)	1 / 3 (33.33%)	0 / 3 (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

Serious adverse events	Pembrolizumab + Placebo (First Course)		
Total subjects affected by serious adverse events			
subjects affected / exposed	92 / 253 (36.36%)		
number of deaths (all causes)	167		
number of deaths resulting from adverse events	23		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Oral haemangioma			
subjects affected / exposed	1 / 253 (0.40%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Leiomyoma			

subjects affected / exposed	1 / 253 (0.40%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Infected neoplasm				
subjects affected / exposed	2 / 253 (0.79%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Bladder transitional cell carcinoma stage 0				
subjects affected / exposed	1 / 253 (0.40%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Basal cell carcinoma				
subjects affected / exposed	1 / 253 (0.40%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Oropharyngeal squamous cell carcinoma				
subjects affected / exposed	1 / 253 (0.40%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Squamous cell carcinoma of skin				
subjects affected / exposed	1 / 253 (0.40%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Tumour pain				
subjects affected / exposed	0 / 253 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Tumour haemorrhage				
subjects affected / exposed	8 / 253 (3.16%)			
occurrences causally related to treatment / all	3 / 9			
deaths causally related to treatment / all	1 / 2			
Vascular disorders				

Arterial haemorrhage				
subjects affected / exposed	0 / 253 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Embolism				
subjects affected / exposed	0 / 253 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypertension				
subjects affected / exposed	0 / 253 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypotension				
subjects affected / exposed	0 / 253 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Orthostatic hypotension				
subjects affected / exposed	0 / 253 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vascular occlusion				
subjects affected / exposed	0 / 253 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Peripheral arterial occlusive disease				
subjects affected / exposed	0 / 253 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
General disorders and administration site conditions				
Asthenia				
subjects affected / exposed	0 / 253 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Death				
subjects affected / exposed	3 / 253 (1.19%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 3			
Pyrexia				
subjects affected / exposed	0 / 253 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
General physical health deterioration				
subjects affected / exposed	2 / 253 (0.79%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 1			
Malaise				
subjects affected / exposed	1 / 253 (0.40%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Mucosal inflammation				
subjects affected / exposed	0 / 253 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pain				
subjects affected / exposed	1 / 253 (0.40%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Fatigue				
subjects affected / exposed	1 / 253 (0.40%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Immune system disorders				
Hypersensitivity				
subjects affected / exposed	1 / 253 (0.40%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Reproductive system and breast				

disorders			
Prostatitis			
subjects affected / exposed	1 / 253 (0.40%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Aspiration			
subjects affected / exposed	0 / 253 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Apnoea			
subjects affected / exposed	1 / 253 (0.40%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Acute respiratory failure			
subjects affected / exposed	1 / 253 (0.40%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Acute respiratory distress syndrome			
subjects affected / exposed	1 / 253 (0.40%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Acquired tracheo-oesophageal fistula			
subjects affected / exposed	1 / 253 (0.40%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Laryngeal stenosis			
subjects affected / exposed	0 / 253 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Immune-mediated lung disease			
subjects affected / exposed	1 / 253 (0.40%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

Haemoptysis			
subjects affected / exposed	0 / 253 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Epistaxis			
subjects affected / exposed	1 / 253 (0.40%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Autoimmune lung disease			
subjects affected / exposed	1 / 253 (0.40%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	1 / 1		
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 253 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Bronchopleural fistula			
subjects affected / exposed	0 / 253 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Bronchial obstruction			
subjects affected / exposed	0 / 253 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Dyspnoea			
subjects affected / exposed	1 / 253 (0.40%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Oropharyngeal fistula			
subjects affected / exposed	0 / 253 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Oropharyngeal pain			

subjects affected / exposed	0 / 253 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pharyngeal haemorrhage				
subjects affected / exposed	0 / 253 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pleural effusion				
subjects affected / exposed	1 / 253 (0.40%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pleurisy				
subjects affected / exposed	1 / 253 (0.40%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumomediastinum				
subjects affected / exposed	1 / 253 (0.40%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonitis				
subjects affected / exposed	6 / 253 (2.37%)			
occurrences causally related to treatment / all	6 / 6			
deaths causally related to treatment / all	0 / 0			
Pneumothorax				
subjects affected / exposed	0 / 253 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pulmonary embolism				
subjects affected / exposed	2 / 253 (0.79%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Obstructive airways disorder				

subjects affected / exposed	2 / 253 (0.79%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 1			
Pulmonary haemorrhage				
subjects affected / exposed	1 / 253 (0.40%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Respiratory failure				
subjects affected / exposed	1 / 253 (0.40%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Tracheal fistula				
subjects affected / exposed	0 / 253 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Psychiatric disorders				
Delirium				
subjects affected / exposed	0 / 253 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Alcohol withdrawal syndrome				
subjects affected / exposed	1 / 253 (0.40%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Confusional state				
subjects affected / exposed	1 / 253 (0.40%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Product issues				
Device occlusion				
subjects affected / exposed	0 / 253 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Device dislocation				

subjects affected / exposed	0 / 253 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Investigations			
Weight decreased			
subjects affected / exposed	0 / 253 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Platelet count decreased			
subjects affected / exposed	0 / 253 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood urea increased			
subjects affected / exposed	0 / 253 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Concussion			
subjects affected / exposed	0 / 253 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Post procedural haemorrhage			
subjects affected / exposed	0 / 253 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Osteoradionecrosis			
subjects affected / exposed	0 / 253 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Humerus fracture			
subjects affected / exposed	0 / 253 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Head injury				
subjects affected / exposed	0 / 253 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Tracheal obstruction				
subjects affected / exposed	1 / 253 (0.40%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Fibula fracture				
subjects affected / exposed	1 / 253 (0.40%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Contusion				
subjects affected / exposed	0 / 253 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Radiation necrosis				
subjects affected / exposed	1 / 253 (0.40%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Stoma site haemorrhage				
subjects affected / exposed	0 / 253 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastrostomy tube site complication				
subjects affected / exposed	1 / 253 (0.40%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Wound complication				
subjects affected / exposed	0 / 253 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vascular pseudoaneurysm				

subjects affected / exposed	0 / 253 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Congenital, familial and genetic disorders			
Tracheo-oesophageal fistula			
subjects affected / exposed	1 / 253 (0.40%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Bradyarrhythmia			
subjects affected / exposed	1 / 253 (0.40%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Acute myocardial infarction			
subjects affected / exposed	0 / 253 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Atrial fibrillation			
subjects affected / exposed	0 / 253 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Acute left ventricular failure			
subjects affected / exposed	1 / 253 (0.40%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	1 / 1		
Cardiac arrest			
subjects affected / exposed	1 / 253 (0.40%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Cardiac failure			
subjects affected / exposed	0 / 253 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Cardiovascular disorder			
subjects affected / exposed	0 / 253 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac tamponade			
subjects affected / exposed	0 / 253 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiomyopathy			
subjects affected / exposed	0 / 253 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac failure acute			
subjects affected / exposed	0 / 253 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiovascular insufficiency			
subjects affected / exposed	1 / 253 (0.40%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Coronary artery stenosis			
subjects affected / exposed	1 / 253 (0.40%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Myocardial infarction			
subjects affected / exposed	0 / 253 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Sinus node dysfunction			
subjects affected / exposed	0 / 253 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Palpitations			

subjects affected / exposed	0 / 253 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pericardial effusion				
subjects affected / exposed	0 / 253 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Myocarditis				
subjects affected / exposed	0 / 253 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
Cerebral infarction				
subjects affected / exposed	1 / 253 (0.40%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cerebral haemorrhage				
subjects affected / exposed	0 / 253 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Autonomic dysreflexia				
subjects affected / exposed	0 / 253 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cerebral ischaemia				
subjects affected / exposed	0 / 253 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Headache				
subjects affected / exposed	0 / 253 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Haemorrhagic stroke				

subjects affected / exposed	0 / 253 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Diabetic hyperosmolar coma				
subjects affected / exposed	1 / 253 (0.40%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Cerebrovascular accident				
subjects affected / exposed	0 / 253 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ischaemic stroke				
subjects affected / exposed	0 / 253 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Peripheral sensorimotor neuropathy				
subjects affected / exposed	0 / 253 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Spinal cord compression				
subjects affected / exposed	1 / 253 (0.40%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Syncope				
subjects affected / exposed	1 / 253 (0.40%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Blood and lymphatic system disorders				
Anaemia				
subjects affected / exposed	0 / 253 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Febrile bone marrow aplasia				

subjects affected / exposed	0 / 253 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ear and labyrinth disorders				
Vertigo				
subjects affected / exposed	0 / 253 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
Colitis				
subjects affected / exposed	1 / 253 (0.40%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Abdominal pain				
subjects affected / exposed	0 / 253 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Constipation				
subjects affected / exposed	1 / 253 (0.40%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Diarrhoea				
subjects affected / exposed	0 / 253 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Dysphagia				
subjects affected / exposed	6 / 253 (2.37%)			
occurrences causally related to treatment / all	0 / 6			
deaths causally related to treatment / all	0 / 0			
Enteritis				
subjects affected / exposed	0 / 253 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Immune-mediated enterocolitis				

subjects affected / exposed	1 / 253 (0.40%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Gastric haemorrhage				
subjects affected / exposed	0 / 253 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastric ulcer				
subjects affected / exposed	0 / 253 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal haemorrhage				
subjects affected / exposed	0 / 253 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Haematemesis				
subjects affected / exposed	1 / 253 (0.40%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Enterocolitis				
subjects affected / exposed	1 / 253 (0.40%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Intestinal obstruction				
subjects affected / exposed	0 / 253 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Large intestine perforation				
subjects affected / exposed	0 / 253 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lower gastrointestinal haemorrhage				

subjects affected / exposed	0 / 253 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Oesophageal stenosis				
subjects affected / exposed	0 / 253 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Mouth haemorrhage				
subjects affected / exposed	1 / 253 (0.40%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Nausea				
subjects affected / exposed	1 / 253 (0.40%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Melaena				
subjects affected / exposed	0 / 253 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Oesophagitis				
subjects affected / exposed	0 / 253 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Oral pain				
subjects affected / exposed	1 / 253 (0.40%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pancreatic mass				
subjects affected / exposed	1 / 253 (0.40%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Stomatitis				

subjects affected / exposed	0 / 253 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pancreatitis acute				
subjects affected / exposed	0 / 253 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Salivary duct inflammation				
subjects affected / exposed	0 / 253 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Small intestinal obstruction				
subjects affected / exposed	0 / 253 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pancreatitis				
subjects affected / exposed	2 / 253 (0.79%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Upper gastrointestinal haemorrhage				
subjects affected / exposed	1 / 253 (0.40%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Vomiting				
subjects affected / exposed	0 / 253 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hepatobiliary disorders				
Cholangitis				
subjects affected / exposed	0 / 253 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cholangitis acute				

subjects affected / exposed	0 / 253 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cholecystitis				
subjects affected / exposed	0 / 253 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cholecystitis acute				
subjects affected / exposed	0 / 253 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hepatitis				
subjects affected / exposed	0 / 253 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypertransaminasaemia				
subjects affected / exposed	0 / 253 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Liver injury				
subjects affected / exposed	0 / 253 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hepatic failure				
subjects affected / exposed	1 / 253 (0.40%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Skin and subcutaneous tissue disorders				
Dermatitis				
subjects affected / exposed	0 / 253 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Drug eruption				

subjects affected / exposed	0 / 253 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Skin ulcer				
subjects affected / exposed	0 / 253 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Renal and urinary disorders				
Nephrotic syndrome				
subjects affected / exposed	0 / 253 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Urinary retention				
subjects affected / exposed	1 / 253 (0.40%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Renal impairment				
subjects affected / exposed	0 / 253 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Endocrine disorders				
Adrenal insufficiency				
subjects affected / exposed	1 / 253 (0.40%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Hypercalcaemia of malignancy				
subjects affected / exposed	1 / 253 (0.40%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Hypopituitarism				
subjects affected / exposed	1 / 253 (0.40%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Hypothyroidism				

subjects affected / exposed	0 / 253 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Inappropriate antidiuretic hormone secretion				
subjects affected / exposed	0 / 253 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hyperthyroidism				
subjects affected / exposed	0 / 253 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal and connective tissue disorders				
Arthritis				
subjects affected / exposed	1 / 253 (0.40%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Soft tissue swelling				
subjects affected / exposed	1 / 253 (0.40%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Scleroderma				
subjects affected / exposed	1 / 253 (0.40%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Osteonecrosis of jaw				
subjects affected / exposed	0 / 253 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Neck pain				
subjects affected / exposed	1 / 253 (0.40%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Haematoma muscle				

subjects affected / exposed	1 / 253 (0.40%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Flank pain				
subjects affected / exposed	1 / 253 (0.40%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Fistula				
subjects affected / exposed	0 / 253 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Trismus				
subjects affected / exposed	0 / 253 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Abdominal abscess				
subjects affected / exposed	0 / 253 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Abdominal infection				
subjects affected / exposed	0 / 253 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Abscess neck				
subjects affected / exposed	0 / 253 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Anal abscess				
subjects affected / exposed	0 / 253 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Appendicitis				

subjects affected / exposed	1 / 253 (0.40%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cellulitis				
subjects affected / exposed	1 / 253 (0.40%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Bronchitis				
subjects affected / exposed	0 / 253 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
COVID-19				
subjects affected / exposed	3 / 253 (1.19%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 1			
COVID-19 pneumonia				
subjects affected / exposed	2 / 253 (0.79%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Catheter site infection				
subjects affected / exposed	0 / 253 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Appendicitis perforated				
subjects affected / exposed	0 / 253 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cystitis				
subjects affected / exposed	1 / 253 (0.40%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Empyema				

subjects affected / exposed	0 / 253 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Fournier's gangrene				
subjects affected / exposed	0 / 253 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis				
subjects affected / exposed	0 / 253 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Perirectal abscess				
subjects affected / exposed	0 / 253 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lung abscess				
subjects affected / exposed	0 / 253 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Necrotising soft tissue infection				
subjects affected / exposed	0 / 253 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Perineal abscess				
subjects affected / exposed	0 / 253 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Infected skin ulcer				
subjects affected / exposed	0 / 253 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pharyngitis				

subjects affected / exposed	0 / 253 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumococcal infection				
subjects affected / exposed	0 / 253 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia				
subjects affected / exposed	13 / 253 (5.14%)			
occurrences causally related to treatment / all	0 / 14			
deaths causally related to treatment / all	0 / 3			
Pneumonia acinetobacter				
subjects affected / exposed	0 / 253 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Rectal abscess				
subjects affected / exposed	0 / 253 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia bacterial				
subjects affected / exposed	0 / 253 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia necrotising				
subjects affected / exposed	0 / 253 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia viral				
subjects affected / exposed	0 / 253 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Rash pustular				

subjects affected / exposed	1 / 253 (0.40%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia aspiration				
subjects affected / exposed	4 / 253 (1.58%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 1			
Respiratory tract infection				
subjects affected / exposed	1 / 253 (0.40%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Sepsis				
subjects affected / exposed	1 / 253 (0.40%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Skin infection				
subjects affected / exposed	0 / 253 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Stoma site infection				
subjects affected / exposed	0 / 253 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Tracheitis				
subjects affected / exposed	0 / 253 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Upper respiratory tract infection				
subjects affected / exposed	0 / 253 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Urinary tract infection				

subjects affected / exposed	0 / 253 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Urosepsis				
subjects affected / exposed	1 / 253 (0.40%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Metabolism and nutrition disorders				
Dehydration				
subjects affected / exposed	0 / 253 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Decreased appetite				
subjects affected / exposed	0 / 253 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Diabetic ketoacidosis				
subjects affected / exposed	1 / 253 (0.40%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Fulminant type 1 diabetes mellitus				
subjects affected / exposed	0 / 253 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypercalcaemia				
subjects affected / exposed	2 / 253 (0.79%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Hyperglycaemia				
subjects affected / exposed	1 / 253 (0.40%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Type 2 diabetes mellitus				

subjects affected / exposed	1 / 253 (0.40%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Malnutrition			
subjects affected / exposed	1 / 253 (0.40%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hyponatraemia			
subjects affected / exposed	2 / 253 (0.79%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Hypokalaemia			
subjects affected / exposed	1 / 253 (0.40%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hypoalbuminaemia			
subjects affected / exposed	0 / 253 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hyperkalaemia			
subjects affected / exposed	0 / 253 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Pembrolizumab + Lenvatinib (First Course)	Pembrolizumab + Placebo (Second Course)	Pembrolizumab + Lenvatinib (Second Course)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	245 / 254 (96.46%)	2 / 3 (66.67%)	3 / 3 (100.00%)
Vascular disorders			
Hypertension			
subjects affected / exposed	117 / 254 (46.06%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	208	0	0

Hypotension			
subjects affected / exposed	15 / 254 (5.91%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	16	0	1
General disorders and administration site conditions			
Mucosal inflammation			
subjects affected / exposed	26 / 254 (10.24%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	36	0	0
Fatigue			
subjects affected / exposed	80 / 254 (31.50%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	92	0	1
Asthenia			
subjects affected / exposed	26 / 254 (10.24%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	32	0	1
Pyrexia			
subjects affected / exposed	21 / 254 (8.27%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	23	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	40 / 254 (15.75%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	47	0	1
Dysphonia			
subjects affected / exposed	23 / 254 (9.06%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	26	0	0
Dyspnoea			
subjects affected / exposed	26 / 254 (10.24%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	34	0	0
Haemoptysis			
subjects affected / exposed	10 / 254 (3.94%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	18	0	1
Oropharyngeal pain			
subjects affected / exposed	28 / 254 (11.02%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	33	0	0
Pneumonitis			
subjects affected / exposed	11 / 254 (4.33%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	12	0	1
Productive cough			

subjects affected / exposed	17 / 254 (6.69%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	18	0	0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	25 / 254 (9.84%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	27	0	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	36 / 254 (14.17%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	49	0	0
Amylase increased			
subjects affected / exposed	15 / 254 (5.91%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	22	0	0
Aspartate aminotransferase increased			
subjects affected / exposed	37 / 254 (14.57%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	58	0	0
Blood alkaline phosphatase increased			
subjects affected / exposed	13 / 254 (5.12%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	15	0	0
Blood bilirubin increased			
subjects affected / exposed	17 / 254 (6.69%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	20	0	0
Blood creatinine increased			
subjects affected / exposed	26 / 254 (10.24%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	28	0	0
Blood thyroid stimulating hormone increased			
subjects affected / exposed	17 / 254 (6.69%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	22	0	0
Lipase increased			
subjects affected / exposed	32 / 254 (12.60%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	40	0	0
Lymphocyte count decreased			
subjects affected / exposed	30 / 254 (11.81%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	59	0	0
Platelet count decreased			

subjects affected / exposed	33 / 254 (12.99%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	47	0	0
Weight decreased			
subjects affected / exposed	65 / 254 (25.59%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	74	0	0
White blood cell count decreased			
subjects affected / exposed	16 / 254 (6.30%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	34	0	0
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	3 / 254 (1.18%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	3	0	1
Nervous system disorders			
Headache			
subjects affected / exposed	32 / 254 (12.60%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	37	0	0
Dizziness			
subjects affected / exposed	13 / 254 (5.12%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	18	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	66 / 254 (25.98%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	102	1	0
Ear and labyrinth disorders			
Deafness			
subjects affected / exposed	1 / 254 (0.39%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Ear pain			
subjects affected / exposed	7 / 254 (2.76%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	7	0	1
Gastrointestinal disorders			
Salivary gland pain			
subjects affected / exposed	0 / 254 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Oral pain			

subjects affected / exposed	30 / 254 (11.81%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	35	0	0
Nausea			
subjects affected / exposed	62 / 254 (24.41%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	83	0	0
Flatulence			
subjects affected / exposed	2 / 254 (0.79%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	2	0	1
Dysphagia			
subjects affected / exposed	36 / 254 (14.17%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	40	0	0
Dyspepsia			
subjects affected / exposed	14 / 254 (5.51%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	22	0	0
Dry mouth			
subjects affected / exposed	18 / 254 (7.09%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	19	0	0
Diarrhoea			
subjects affected / exposed	73 / 254 (28.74%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	117	0	1
Constipation			
subjects affected / exposed	57 / 254 (22.44%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	74	0	0
Bowel movement irregularity			
subjects affected / exposed	0 / 254 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Vomiting			
subjects affected / exposed	33 / 254 (12.99%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	48	0	0
Stomatitis			
subjects affected / exposed	52 / 254 (20.47%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	74	0	0
Skin and subcutaneous tissue disorders			
Dry skin			
subjects affected / exposed	15 / 254 (5.91%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	15	0	0

Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	36 / 254 (14.17%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	51	0	0
Pruritus			
subjects affected / exposed	29 / 254 (11.42%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	35	0	0
Rash			
subjects affected / exposed	34 / 254 (13.39%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	47	0	0
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	13 / 254 (5.12%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	20	0	0
Proteinuria			
subjects affected / exposed	66 / 254 (25.98%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	125	0	0
Endocrine disorders			
Hyperthyroidism			
subjects affected / exposed	19 / 254 (7.48%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	23	0	0
Hypothyroidism			
subjects affected / exposed	125 / 254 (49.21%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	151	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	40 / 254 (15.75%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	51	1	0
Musculoskeletal chest pain			
subjects affected / exposed	8 / 254 (3.15%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	8	0	1
Neck pain			
subjects affected / exposed	18 / 254 (7.09%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	18	0	0
Infections and infestations			
Urinary tract infection			

subjects affected / exposed	13 / 254 (5.12%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	18	0	0
Pneumonia			
subjects affected / exposed	26 / 254 (10.24%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	27	0	0
COVID-19			
subjects affected / exposed	17 / 254 (6.69%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	18	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	57 / 254 (22.44%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	70	0	1
Hypercalcaemia			
subjects affected / exposed	12 / 254 (4.72%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	15	0	0
Hyperglycaemia			
subjects affected / exposed	16 / 254 (6.30%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	25	0	0
Hypoalbuminaemia			
subjects affected / exposed	34 / 254 (13.39%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	47	0	0
Hyperkalaemia			
subjects affected / exposed	18 / 254 (7.09%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	20	1	0
Hypokalaemia			
subjects affected / exposed	22 / 254 (8.66%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	29	0	0
Hypomagnesaemia			
subjects affected / exposed	22 / 254 (8.66%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	31	0	0
Hyponatraemia			
subjects affected / exposed	47 / 254 (18.50%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	75	0	0
Hypophosphataemia			
subjects affected / exposed	14 / 254 (5.51%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	16	0	0

Non-serious adverse events	Pembrolizumab + Placebo (First Course)		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	222 / 253 (87.75%)		
Vascular disorders			
Hypertension			
subjects affected / exposed	25 / 253 (9.88%)		
occurrences (all)	42		
Hypotension			
subjects affected / exposed	7 / 253 (2.77%)		
occurrences (all)	8		
General disorders and administration site conditions			
Mucosal inflammation			
subjects affected / exposed	7 / 253 (2.77%)		
occurrences (all)	10		
Fatigue			
subjects affected / exposed	43 / 253 (17.00%)		
occurrences (all)	46		
Asthenia			
subjects affected / exposed	25 / 253 (9.88%)		
occurrences (all)	30		
Pyrexia			
subjects affected / exposed	20 / 253 (7.91%)		
occurrences (all)	25		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	24 / 253 (9.49%)		
occurrences (all)	26		
Dysphonia			
subjects affected / exposed	4 / 253 (1.58%)		
occurrences (all)	4		
Dyspnoea			
subjects affected / exposed	15 / 253 (5.93%)		
occurrences (all)	15		
Haemoptysis			

subjects affected / exposed occurrences (all)	10 / 253 (3.95%) 12		
Oropharyngeal pain subjects affected / exposed occurrences (all)	9 / 253 (3.56%) 9		
Pneumonitis subjects affected / exposed occurrences (all)	10 / 253 (3.95%) 10		
Productive cough subjects affected / exposed occurrences (all)	7 / 253 (2.77%) 7		
Psychiatric disorders Insomnia subjects affected / exposed occurrences (all)	12 / 253 (4.74%) 13		
Investigations Alanine aminotransferase increased subjects affected / exposed occurrences (all)	22 / 253 (8.70%) 29		
Amylase increased subjects affected / exposed occurrences (all)	14 / 253 (5.53%) 21		
Aspartate aminotransferase increased subjects affected / exposed occurrences (all)	23 / 253 (9.09%) 36		
Blood alkaline phosphatase increased subjects affected / exposed occurrences (all)	20 / 253 (7.91%) 25		
Blood bilirubin increased subjects affected / exposed occurrences (all)	7 / 253 (2.77%) 10		
Blood creatinine increased subjects affected / exposed occurrences (all)	7 / 253 (2.77%) 9		
Blood thyroid stimulating hormone increased			

subjects affected / exposed occurrences (all) Lipase increased subjects affected / exposed occurrences (all) Lymphocyte count decreased subjects affected / exposed occurrences (all) Platelet count decreased subjects affected / exposed occurrences (all) Weight decreased subjects affected / exposed occurrences (all) White blood cell count decreased subjects affected / exposed occurrences (all)	7 / 253 (2.77%) 7 18 / 253 (7.11%) 33 23 / 253 (9.09%) 45 8 / 253 (3.16%) 13 41 / 253 (16.21%) 43 11 / 253 (4.35%) 17		
Injury, poisoning and procedural complications Fall subjects affected / exposed occurrences (all)	4 / 253 (1.58%) 4		
Nervous system disorders Headache subjects affected / exposed occurrences (all) Dizziness subjects affected / exposed occurrences (all)	16 / 253 (6.32%) 16 8 / 253 (3.16%) 8		
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all)	52 / 253 (20.55%) 75		
Ear and labyrinth disorders Deafness subjects affected / exposed occurrences (all)	1 / 253 (0.40%) 1		

Ear pain			
subjects affected / exposed	3 / 253 (1.19%)		
occurrences (all)	3		
Gastrointestinal disorders			
Salivary gland pain			
subjects affected / exposed	0 / 253 (0.00%)		
occurrences (all)	0		
Oral pain			
subjects affected / exposed	7 / 253 (2.77%)		
occurrences (all)	8		
Nausea			
subjects affected / exposed	26 / 253 (10.28%)		
occurrences (all)	28		
Flatulence			
subjects affected / exposed	1 / 253 (0.40%)		
occurrences (all)	1		
Dysphagia			
subjects affected / exposed	14 / 253 (5.53%)		
occurrences (all)	15		
Dyspepsia			
subjects affected / exposed	3 / 253 (1.19%)		
occurrences (all)	3		
Dry mouth			
subjects affected / exposed	18 / 253 (7.11%)		
occurrences (all)	19		
Diarrhoea			
subjects affected / exposed	34 / 253 (13.44%)		
occurrences (all)	46		
Constipation			
subjects affected / exposed	47 / 253 (18.58%)		
occurrences (all)	57		
Bowel movement irregularity			
subjects affected / exposed	0 / 253 (0.00%)		
occurrences (all)	0		
Vomiting			

subjects affected / exposed	14 / 253 (5.53%)		
occurrences (all)	16		
Stomatitis			
subjects affected / exposed	12 / 253 (4.74%)		
occurrences (all)	12		
Skin and subcutaneous tissue disorders			
Dry skin			
subjects affected / exposed	8 / 253 (3.16%)		
occurrences (all)	8		
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	2 / 253 (0.79%)		
occurrences (all)	2		
Pruritus			
subjects affected / exposed	30 / 253 (11.86%)		
occurrences (all)	43		
Rash			
subjects affected / exposed	26 / 253 (10.28%)		
occurrences (all)	29		
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	7 / 253 (2.77%)		
occurrences (all)	11		
Proteinuria			
subjects affected / exposed	16 / 253 (6.32%)		
occurrences (all)	17		
Endocrine disorders			
Hyperthyroidism			
subjects affected / exposed	10 / 253 (3.95%)		
occurrences (all)	10		
Hypothyroidism			
subjects affected / exposed	43 / 253 (17.00%)		
occurrences (all)	52		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	18 / 253 (7.11%)		
occurrences (all)	25		

Musculoskeletal chest pain subjects affected / exposed occurrences (all)	3 / 253 (1.19%) 5		
Neck pain subjects affected / exposed occurrences (all)	9 / 253 (3.56%) 10		
Infections and infestations Urinary tract infection subjects affected / exposed occurrences (all)	13 / 253 (5.14%) 17		
Pneumonia subjects affected / exposed occurrences (all)	12 / 253 (4.74%) 13		
COVID-19 subjects affected / exposed occurrences (all)	14 / 253 (5.53%) 14		
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	23 / 253 (9.09%) 25		
Hypercalcaemia subjects affected / exposed occurrences (all)	18 / 253 (7.11%) 20		
Hyperglycaemia subjects affected / exposed occurrences (all)	12 / 253 (4.74%) 13		
Hypoalbuminaemia subjects affected / exposed occurrences (all)	24 / 253 (9.49%) 26		
Hyperkalaemia subjects affected / exposed occurrences (all)	7 / 253 (2.77%) 8		
Hypokalaemia subjects affected / exposed occurrences (all)	9 / 253 (3.56%) 11		
Hypomagnesaemia			

subjects affected / exposed	11 / 253 (4.35%)		
occurrences (all)	14		
Hyponatraemia			
subjects affected / exposed	29 / 253 (11.46%)		
occurrences (all)	38		
Hypophosphataemia			
subjects affected / exposed	4 / 253 (1.58%)		
occurrences (all)	4		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
20 July 2020	Amendment 02: Primary reason for amendment was to incorporate Health Authority feedback, amend exclusion criteria, and provide program-level corrections and clarifications.
26 July 2021	Amendment 03: Primary reason for amendment was to update the dose modification and toxicity management guidelines for immune-related Adverse Events (irAEs).
23 August 2022	Amendment 04: Primary reason for amendment was to address an entity name and address change.
04 December 2023	Amendment 05: Primary reason for amendment was to terminate the study based on interim analysis results and incorporate instructions for discontinuation of study intervention, appropriate measures for safety follow-up of ongoing study participants, and plan for analysis of study data going forward.
11 October 2024	Amendment 06: Primary reason for amendment was to correct standard text inadvertently removed in Amendment 05.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported