



## Clinical trial results:

### A Phase 3 Randomized, Placebo-controlled Study to Evaluate the Safety and Efficacy of Pemetrexed + Platinum Chemotherapy + Pembrolizumab (MK-3475) with or without Lenvatinib (E7080/MK-7902) as First-line Intervention in Participants with Metastatic Nonsquamous Non-small Cell Lung Cancer (LEAP-006)

#### Summary

EudraCT number	2018-003824-35
Trial protocol	GB DE ES PL FR
Global end of trial date	30 August 2024

#### Results information

Result version number	v1 (current)
This version publication date	05 September 2025
First version publication date	05 September 2025

#### Trial information

##### Trial identification

Sponsor protocol code	MK-7902-006
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##### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03829319
WHO universal trial number (UTN)	-

Notes:

#### Sponsors

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

Notes:

#### Paediatric regulatory details

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

Notes:

## Results analysis stage

Analysis stage	Final
Date of interim/final analysis	30 August 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	11 August 2023
Global end of trial reached?	Yes
Global end of trial date	30 August 2024
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

The purpose of this study is to assess the safety and efficacy of pemetrexed + platinum chemotherapy + pembrolizumab (MK-3475) with or without lenvatinib (MK-7902/E7080) as first-line intervention in adults with metastatic nonsquamous non-small cell lung cancer.

The primary study hypotheses state that: 1) the combination of lenvatinib + platinum doublet chemotherapy + pembrolizumab prolongs Progression-free Survival (PFS) as assessed by blinded independent central review (BICR) per modified Response Evaluation Criteria in Solid Tumors version 1.1 (RESIST 1.1) compared to matching placebo + platinum doublet chemotherapy + pembrolizumab, and 2) the combination of lenvatinib + platinum doublet chemotherapy + pembrolizumab prolongs Overall Survival (OS) compared to matching placebo + platinum doublet chemotherapy + pembrolizumab.

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	25 March 2019
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

## Population of trial subjects

### Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 55
Country: Number of subjects enrolled	Australia: 16
Country: Number of subjects enrolled	Canada: 17
Country: Number of subjects enrolled	Chile: 74
Country: Number of subjects enrolled	China: 134
Country: Number of subjects enrolled	Germany: 19
Country: Number of subjects enrolled	Spain: 110
Country: Number of subjects enrolled	France: 26
Country: Number of subjects enrolled	United Kingdom: 21
Country: Number of subjects enrolled	Israel: 36
Country: Number of subjects enrolled	Japan: 50
Country: Number of subjects enrolled	Korea, Democratic People's Republic of: 42
Country: Number of subjects enrolled	New Zealand: 4
Country: Number of subjects enrolled	Poland: 33

Country: Number of subjects enrolled	Russian Federation: 47
Country: Number of subjects enrolled	Türkiye: 59
Country: Number of subjects enrolled	United States: 18
Worldwide total number of subjects	761
EEA total number of subjects	188

Notes:

<b>Subjects enrolled per age group</b>	
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)	415
From 65 to 84 years	343
85 years and over	3

## Subject disposition

### Recruitment

Recruitment details:

Participants with treatment-naïve, metastatic nonsquamous Non-small cell lung cancer (NSCLC) were recruited in this study.

### Pre-assignment

Screening details:

Per protocol, Part 1 participants were excluded from all Part 2 efficacy and safety outcome measures.

### Period 1

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

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	Part 1 First Course: Pembrolizumab+Chemotherapy+Lenvatinib

Arm description:

Participants received carboplatin AUC5 or cisplatin 75 mg/m<sup>2</sup> via IV infusion Q3W for 4 cycles PLUS pemetrexed 500 mg/m<sup>2</sup> via IV infusion Q3W for 4 cycles PLUS pembrolizumab 200 mg via IV infusion Q3W for up to 35 cycles (up to 2 years) PLUS lenvatinib 8 mg via oral capsule once daily.

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:

200 mg via intravenous (IV) infusion on Day 1 of each 3-week cycle (Q3W) for up to 35 administrations (up to approximately 2 years)

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

Dosage and administration details:

8 mg via oral capsule once daily (QD) on Days 1-21 of each 3-week cycle until progressive disease or unacceptable toxicity or intercurrent illness that prevents further administration of treatment or investigator's decision to withdraw treatment or participant withdrawal of consent or pregnancy or noncompliance with study intervention or procedure requirements, or administrative reasons requiring cessation of treatment

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

Dosage and administration details:

500 mg/m<sup>2</sup> via IV infusion Q3W for 4 cycles until progressive disease or unacceptable toxicity or intercurrent illness that prevents further administration of treatment or investigator's decision to withdraw treatment or participant withdrawal of consent or pregnancy or noncompliance with study intervention or procedure requirements, or administrative reasons requiring cessation of treatment

Investigational medicinal product name	Cisplatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use
Dosage and administration details:	
5 mg/m <sup>2</sup> via IV infusion on Day 1 of each Q3W for 4 cycles (up to approximately 2 years)	
Investigational medicinal product name	Carboplatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use
Dosage and administration details:	
Area Under Curve 5 mg/mL/min (AUC5) IV infusion on Day 1 of each Q3W for 4 cycles (up to approximately 2 years)	
<b>Arm title</b>	Part 2 First Course: Pembrolizumab+Chemotherapy+Lenvatinib
Arm description:	
Participants received carboplatin Area Under Curve 5 mg/mL/min (AUC5) or cisplatin 75 mg/m <sup>2</sup> via intravenous (IV) infusion on Day 1 of each 3-week cycle (Q3W) for 4 cycles PLUS pemetrexed 500 mg/m <sup>2</sup> via IV infusion Q3W for 4 cycles PLUS pembrolizumab 200 mg via IV infusion Q3W for up to 35 cycles (up to 2 years) PLUS lenvatinib 8 mg via oral capsule once daily.	
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:	
200 mg via intravenous (IV) infusion on Day 1 of each 3-week cycle (Q3W) for up to 35 administrations (up to approximately 2 years)	
Investigational medicinal product name	Lenvatinib
Investigational medicinal product code	
Other name	MK-7902 E7080 LENVIMA®
Pharmaceutical forms	Capsule
Routes of administration	Oral use
Dosage and administration details:	
8 mg via oral capsule once daily (QD) on Days 1-21 of each 3-week cycle until progressive disease or unacceptable toxicity or intercurrent illness that prevents further administration of treatment or investigator's decision to withdraw treatment or participant withdrawal of consent or pregnancy or noncompliance with study intervention or procedure requirements, or administrative reasons requiring cessation of treatment	
Investigational medicinal product name	Carboplatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use
Dosage and administration details:	
Area Under Curve 5 mg/mL/min (AUC5) IV infusion on Day 1 of each Q3W for 4 cycles (up to approximately 2 years)	
Investigational medicinal product name	Cisplatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details: 5 mg/m <sup>2</sup> via IV infusion on Day 1 of each Q3W for 4 cycles (up to approximately 2 years)	
Investigational medicinal product name	Pemetrexed
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use
Dosage and administration details: 500 mg/m <sup>2</sup> via IV infusion Q3W for 4 cycles until progressive disease or unacceptable toxicity or intercurrent illness that prevents further administration of treatment or investigator's decision to withdraw treatment or participant withdrawal of consent or pregnancy or noncompliance with study intervention or procedure requirements, or administrative reasons requiring cessation of treatment	
<b>Arm title</b>	Part 2 First Course: Pembrolizumab+Chemotherapy+Placebo
Arm description: Participants received carboplatin AUC5 or cisplatin 75 mg/m <sup>2</sup> via IV infusion Q3W for 4 cycles PLUS pemetrexed 500 mg/m <sup>2</sup> via IV infusion Q3W for 4 cycles PLUS pembrolizumab 200 mg via IV infusion Q3W for up to 35 cycles (up to 2 years) PLUS placebo matching lenvatinib via oral capsule once daily.	
Arm type	Placebo
Investigational medicinal product name	Lenvatinib
Investigational medicinal product code	
Other name	MK-7902 E7080 LENVIMA®
Pharmaceutical forms	Capsule
Routes of administration	Oral use
Dosage and administration details: 8 mg via oral capsule once daily (QD) on Days 1-21 of each 3-week cycle until progressive disease or unacceptable toxicity or intercurrent illness that prevents further administration of treatment or investigator's decision to withdraw treatment or participant withdrawal of consent or pregnancy or noncompliance with study intervention or procedure requirements, or administrative reasons requiring cessation of treatment	
Investigational medicinal product name	Carboplatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use
Dosage and administration details: Area Under Curve 5 mg/mL/min (AUC5) IV infusion on Day 1 of each Q3W for 4 cycles (up to approximately 2 years)	
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: 200 mg via intravenous (IV) infusion on Day 1 of each 3-week cycle (Q3W) for up to 35 administrations (up to approximately 2 years)	
Investigational medicinal product name	Pemetrexed
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use
Dosage and administration details: 500 mg/m <sup>2</sup> via IV infusion Q3W for 4 cycles until progressive disease or unacceptable toxicity or intercurrent illness that prevents further administration of treatment or investigator's decision to withdraw treatment or participant withdrawal of consent or pregnancy or noncompliance with study intervention or procedure requirements, or administrative reasons requiring cessation of treatment	

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

Dosage and administration details:

oral capsule QD on Days 1-21 of each Q3W until progressive disease or unacceptable toxicity or intercurrent illness that prevents further administration of treatment or investigator's decision to withdraw treatment or participant withdrawal of consent or pregnancy or noncompliance with study intervention or procedure requirements, or administrative reasons requiring cessation of treatment

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

Dosage and administration details:

5 mg/m<sup>2</sup> via IV infusion on Day 1 of each Q3W for 4 cycles (up to approximately 2 years)

<b>Number of subjects in period 1</b>	Part 1 First Course: Pembrolizumab+Chemotherapy+Lenvatinib	Part 2 First Course: Pembrolizumab+Chemotherapy+Lenvatinib	Part 2 First Course: Pembrolizumab+Chemotherapy+Placebo
Started	13	375	373
Treated during first course	13	373	372
Treated during second Course	1	3	5
Completed	0	0	0
Not completed	13	375	373
Adverse event, serious fatal	8	277	266
Consent withdrawn by subject	1	5	4
Physician decision	-	3	-
Sponsor's Decision	4	90	102
Lost to follow-up	-	-	1

## Baseline characteristics

### Reporting groups

Reporting group title	Part 1 First Course: Pembrolizumab+Chemotherapy+Lenvatinib
Reporting group description:	
Participants received carboplatin AUC5 or cisplatin 75 mg/m <sup>2</sup> via IV infusion Q3W for 4 cycles PLUS pemetrexed 500 mg/m <sup>2</sup> via IV infusion Q3W for 4 cycles PLUS pembrolizumab 200 mg via IV infusion Q3W for up to 35 cycles (up to 2 years) PLUS lenvatinib 8 mg via oral capsule once daily.	
Reporting group title	Part 2 First Course: Pembrolizumab+Chemotherapy+Lenvatinib
Reporting group description:	
Participants received carboplatin Area Under Curve 5 mg/mL/min (AUC5) or cisplatin 75 mg/m <sup>2</sup> via intravenous (IV) infusion on Day 1 of each 3-week cycle (Q3W) for 4 cycles PLUS pemetrexed 500 mg/m <sup>2</sup> via IV infusion Q3W for 4 cycles PLUS pembrolizumab 200 mg via IV infusion Q3W for up to 35 cycles (up to 2 years) PLUS lenvatinib 8 mg via oral capsule once daily.	
Reporting group title	Part 2 First Course: Pembrolizumab+Chemotherapy+Placebo
Reporting group description:	
Participants received carboplatin AUC5 or cisplatin 75 mg/m <sup>2</sup> via IV infusion Q3W for 4 cycles PLUS pemetrexed 500 mg/m <sup>2</sup> via IV infusion Q3W for 4 cycles PLUS pembrolizumab 200 mg via IV infusion Q3W for up to 35 cycles (up to 2 years) PLUS placebo matching lenvatinib via oral capsule once daily.	

Reporting group values	Part 1 First Course: Pembrolizumab+Chemotherapy+Lenvatinib	Part 2 First Course: Pembrolizumab+Chemotherapy+Lenvatinib	Part 2 First Course: Pembrolizumab+Chemotherapy+Placebo
Number of subjects	13	375	373
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age Continuous Units: Years			
arithmetic mean	64.2	62.0	63.0
standard deviation	± 7.6	± 9.9	± 9.7
Sex: Female, Male Units: Participants			
Female	6	121	126
Male	7	254	247
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	1
Asian	5	116	114
Native Hawaiian or Other Pacific Islander	0	2	1
Black or African American	0	0	3



White	8	248	237
More than one race	0	0	0
Unknown or Not Reported	0	9	17
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	0	75	77
Not Hispanic or Latino	13	291	279
Unknown or Not Reported	0	9	17
Eastern Cooperative Oncology Group (ECOG) Performance Status			
Randomization of participants in the study was stratified by an ECOG Performance Status of 0 (Fully active, able to carry on all pre-disease performance without restriction) or 1 (Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature)			
Units: Subjects			
ECOG = 0	8	135	133
ECOG = 1	5	240	240
Programmed Cell Death Ligand 1 (PD-L1) Status at Baseline			
Participants were assessed for their PD-L1 tumor expression level by immunohistochemistry assay using tumor tissue from a newly obtained biopsy. Randomization of participants in the study was stratified by PD-L1 tumor proportion score (TPS) at baseline (< 50% or ≥ 50%). Higher percentages of PD-L1 TPS staining correspond to higher positivity of PD-L1 on a tumor.			
Units: Subjects			
TPS = < 50%	10	272	269
TPS = ≥ 50%	3	90	91
Not Evaluable	0	13	13
Geographic Region			
Randomization of participants in this study was stratified by geographic region of the enrolling site (East Asia or non-East Asia).			
Units: Subjects			
East Asia	3	111	112
Non-East Asia	10	264	261

<b>Reporting group values</b>	Total		
Number of subjects	761		
Age categorical			
Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			
From 65-84 years			
85 years and over			
Age Continuous			
Units: Years			
arithmetic mean			
standard deviation	-		

Sex: Female, Male			
Units: Participants			
Female	253		
Male	508		
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	1		
Asian	235		
Native Hawaiian or Other Pacific Islander	3		
Black or African American	3		
White	493		
More than one race	0		
Unknown or Not Reported	26		
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	152		
Not Hispanic or Latino	583		
Unknown or Not Reported	26		
Eastern Cooperative Oncology Group (ECOG) Performance Status			
Randomization of participants in the study was stratified by an ECOG Performance Status of 0 (Fully active, able to carry on all pre-disease performance without restriction) or 1 (Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature)			
Units: Subjects			
ECOG = 0	276		
ECOG = 1	485		
Programmed Cell Death Ligand 1 (PD-L1) Status at Baseline			
Participants were assessed for their PD-L1 tumor expression level by immunohistochemistry assay using tumor tissue from a newly obtained biopsy. Randomization of participants in the study was stratified by PD-L1 tumor proportion score (TPS) at baseline (< 50% or ≥ 50%). Higher percentages of PD-L1 TPS staining correspond to higher positivity of PD-L1 on a tumor.			
Units: Subjects			
TPS = < 50%	551		
TPS = ≥ 50%	184		
Not Evaluable	26		
Geographic Region			
Randomization of participants in this study was stratified by geographic region of the enrolling site (East Asia or non-East Asia).			
Units: Subjects			
East Asia	226		
Non-East Asia	535		

## End points

### End points reporting groups

Reporting group title	Part 1 First Course: Pembrolizumab+Chemotherapy+Lenvatinib
Reporting group description: Participants received carboplatin AUC5 or cisplatin 75 mg/m <sup>2</sup> via IV infusion Q3W for 4 cycles PLUS pemetrexed 500 mg/m <sup>2</sup> via IV infusion Q3W for 4 cycles PLUS pembrolizumab 200 mg via IV infusion Q3W for up to 35 cycles (up to 2 years) PLUS lenvatinib 8 mg via oral capsule once daily.	
Reporting group title	Part 2 First Course: Pembrolizumab+Chemotherapy+Lenvatinib
Reporting group description: Participants received carboplatin Area Under Curve 5 mg/mL/min (AUC5) or cisplatin 75 mg/m <sup>2</sup> via intravenous (IV) infusion on Day 1 of each 3-week cycle (Q3W) for 4 cycles PLUS pemetrexed 500 mg/m <sup>2</sup> via IV infusion Q3W for 4 cycles PLUS pembrolizumab 200 mg via IV infusion Q3W for up to 35 cycles (up to 2 years) PLUS lenvatinib 8 mg via oral capsule once daily.	
Reporting group title	Part 2 First Course: Pembrolizumab+Chemotherapy+Placebo
Reporting group description: Participants received carboplatin AUC5 or cisplatin 75 mg/m <sup>2</sup> via IV infusion Q3W for 4 cycles PLUS pemetrexed 500 mg/m <sup>2</sup> via IV infusion Q3W for 4 cycles PLUS pembrolizumab 200 mg via IV infusion Q3W for up to 35 cycles (up to 2 years) PLUS placebo matching lenvatinib via oral capsule once daily.	

### Primary: Part 1: Number of Participants Who Experienced an Adverse Event (AE)

End point title	Part 1: Number of Participants Who Experienced an Adverse Event (AE) <sup>[1][2]</sup>
End point description: An adverse event is defined as any untoward medical occurrence in a clinical study participant, temporally associated with the use of study intervention, whether or not considered related to the study intervention. The number of participants who experience one of more adverse events during Part 1 of this study will be presented. The analysis population consisted of all participants enrolled in Part 1 who received at least 1 dose of study intervention.	
End point type	Primary
End point timeframe: Up to approximately 48 months	

#### Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: There are no statistical analyses planned for this endpoint.

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: There are no statistical analyses planned for this endpoint.

<b>End point values</b>	Part 1 First Course: Pembrolizumab+Chemotherapy+Lenvatinib			
Subject group type	Reporting group			
Number of subjects analysed	13			
Units: Participants	13			

### Statistical analyses

**Primary: Part 1: Number of Participants with a Dose-limiting Toxicity (DLT)**

End point title	Part 1: Number of Participants with a Dose-limiting Toxicity (DLT) <sup>[3][4]</sup>
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## End point description:

Dose-limiting toxicity using Common Terminology Criteria for Adverse Events v4.0 for grading, is defined as any of the following hematologic toxicities: 1) Grade 4 neutropenia, 2) Grade 3 or 4 febrile neutropenia, 3) thrombocytopenia <25,000 cells/mm<sup>3</sup> associated with bleeding and/or which requires platelet transfusion, or any of the following non-hematologic toxicities: 4) any other Grade 4 or 5 toxicity, 5) Grade 3 toxicities lasting >3 days (exclusions apply), 6) Grade 3 hypertension not controlled by medication, 7) Grade 3 or above gastrointestinal perforation, 8) Grade 3 or above wound dehiscence requiring medical or surgical intervention, 9) any grade thromboembolic event, or 10) any Grade 3 nonhematologic laboratory value if medical intervention is required or the abnormality leads to hospitalization. The analysis population consisted of all participants enrolled in Part 1 who received at least 1 dose of study intervention.

End point type	Primary
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## End point timeframe:

Cycle 1; each cycle is 21 days (up to 21 days)

## Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: There are no statistical analyses planned for this endpoint.

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: There are no statistical analyses planned for this endpoint.

<b>End point values</b>	Part 1 First Course: Pembrolizumab + Chemotherapy + Lenvatinib			
Subject group type	Reporting group			
Number of subjects analysed	13			
Units: Participants	2			

**Statistical analyses**

No statistical analyses for this end point

**Primary: Part 2: Progression-free Survival (PFS) per Response Evaluation Criteria in Solid Tumors Version 1.1 (RECIST 1.1)**

End point title	Part 2: Progression-free Survival (PFS) per Response Evaluation Criteria in Solid Tumors Version 1.1 (RECIST 1.1) <sup>[5]</sup>
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## End point description:

PFS was defined as the time from date of randomization to the date of the first documentation of progressive disease (PD) or death from any cause, whichever occurred 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 was also considered PD. Data are from the product-limit (Kaplan-Meier) method for censored data. PFS as assessed by blinded independent central review (BICR) per RECIST 1.1 is presented. The analysis population consisted of all randomized participants in Part 2 who received at least 1 dose of study intervention and were evaluable for response.

End point type	Primary
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End point timeframe:

Up to approximately 36 months

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The statistical analysis planned for part 2 first course for this endpoint.

End point values	Part 2 First Course: Pembrolizumab +Chemotherapy +Lenvatinib	Part 2 First Course: Pembrolizumab +Chemotherapy +Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	375	373		
Units: Months				
median (confidence interval 95%)	12.1 (10.4 to 14.1)	9.5 (8.3 to 10.7)		

## Statistical analyses

Statistical analysis title	Hazard Ratio (HR)
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Statistical analysis description:

Comparison based on Cox regression model with Efron's method of tie handling with treatment as a covariate stratified by ECOG performance status (0 versus 1), geographic region of the enrolling site (East Asia versus non-East Asia), and Baseline PD-L1 Status (<50% versus ≥50%).

Comparison groups	Part 2 First Course: Pembrolizumab+Chemotherapy+Lenvatinib v Part 2 First Course: Pembrolizumab+Chemotherapy+Placebo
Number of subjects included in analysis	748
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.07976
Method	Stratified Log Rank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.88
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.74
upper limit	1.05

## Primary: Part 1: Number of Participants Who Discontinued Study Drug Due to an Adverse Event

End point title	Part 1: Number of Participants Who Discontinued Study Drug Due to an Adverse Event <sup>[6][7]</sup>
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End point description:

An adverse event is defined as any untoward medical occurrence in a clinical study participant, temporally associated with the use of study intervention, whether or not considered related to the study intervention. The number of participants who discontinue study medication due to and adverse event during Part 1 of this study will be presented. The analysis population consisted of all participants enrolled in Part 1 who received at least 1 dose of study intervention.

End point type	Primary
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End point timeframe:

Up to approximately 48 months

Notes:

[6] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: There are no statistical analyses planned for this endpoint.

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: There are no statistical analyses planned for this endpoint.

<b>End point values</b>	Part 1 First Course: Pembrolizumab +Chemotherapy+Lenvatinib			
Subject group type	Reporting group			
Number of subjects analysed	13			
Units: Participants	9			

## Statistical analyses

No statistical analyses for this end point

## Primary: Part 2: Overall Survival (OS)

End point title	Part 2: Overall Survival (OS) <sup>[8]</sup>
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End point description:

OS is defined as the time from randomization to the time of death from any cause. OS is presented. The analysis population consisted of all randomized participants in Part 2 who received at least 1 dose of study intervention and were evaluable for response.

End point type	Primary
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End point timeframe:

Up to approximately 47 months

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The statistical analysis planned for part 2 first course for this endpoint.

<b>End point values</b>	Part 2 First Course: Pembrolizumab +Chemotherapy+Lenvatinib	Part 2 First Course: Pembrolizumab +Chemotherapy+Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	375	373		
Units: Months				
median (confidence interval 95%)	21.8 (18.6 to 24.0)	22.1 (19.7 to 24.2)		

## Statistical analyses

<b>Statistical analysis title</b>	Hazard Ratio (HR)
Statistical analysis description:	
Comparison based on Cox regression model with Efron's method of tie handling with treatment as a covariate stratified by ECOG performance status (0 versus 1), geographic region of the enrolling site (East Asia versus non-East Asia), and Baseline PD-L1 Status (<50% versus ≥50%).	
Comparison groups	Part 2 First Course: Pembrolizumab+Chemotherapy+Lenvatinib v Part 2 First Course: Pembrolizumab+Chemotherapy+Placebo
Number of subjects included in analysis	748
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.70818
Method	Stratified Log Rank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.88
upper limit	1.26

## Secondary: Part 2: Objective Response Rate (ORR) per Response Evaluation Criteria in Solid Tumors Version 1.1 (RECIST 1.1)

End point title	Part 2: Objective Response Rate (ORR) per Response Evaluation Criteria in Solid Tumors Version 1.1 (RECIST 1.1) <sup>[9]</sup>
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End point description:

ORR is defined as the percentage of participants in the analysis population who have 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) per RECIST 1.1, modified to follow a maximum of 10 target lesions and a maximum of 5 target lesions per organ. ORR as assessed per modified RECIST 1.1 will be presented. The analysis population consisted of all randomized participants in Part 2 who received at least 1 dose of study intervention and were evaluable for response.

End point type	Secondary
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End point timeframe:

Up to approximately 19 months

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The statistical analysis planned for part 2 first course for this endpoint.

<b>End point values</b>	Part 2 First Course: Pembrolizumab+Chemotherapy+Lenvatinib	Part 2 First Course: Pembrolizumab+Chemotherapy+Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	212	211		
Units: Percentage of Participants				
number (confidence interval 95%)	57.1 (50.1 to 63.8)	50.7 (43.8 to 57.6)		

## Statistical analyses

Statistical analysis title	Percent Difference
Statistical analysis description:	
Comparison based on Miettinen & Nurminen method stratified by ECOG performance status (0 versus 1), geographic region of the enrolling site (East Asia versus non-East Asia), and Baseline PD-L1 Status (<50% versus ≥50% ).	
Comparison groups	Part 2 First Course: Pembrolizumab+Chemotherapy+Lenvatinib v Part 2 First Course: Pembrolizumab+Chemotherapy+Placebo
Number of subjects included in analysis	423
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.08643
Method	Stratified Miettinen & Nurminen
Parameter estimate	Percent Difference
Point estimate	6.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.8
upper limit	15.4

## Secondary: Part 2: Duration of Response (DOR) per Response Evaluation Criteria in Solid Tumors Version 1.1 (RECIST 1.1)

End point title	Part 2: Duration of Response (DOR) per Response Evaluation Criteria in Solid Tumors Version 1.1 (RECIST 1.1) <sup>[10]</sup>
End point description:	
For participants who demonstrated CR (disappearance of all target lesions) or PR (at least a 30% decrease in the sum of diameters of target lesions), DOR is defined as the time from the first documented evidence of CR or PR until PD or death from any cause, whichever occurs first. Per RECIST 1.1 modified to follow a maximum of 10 target lesions and a maximum of 5 target lesions per organ, or death from any cause, PD is 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. DOR as assessed per modified RECIST 1.1 will be presented. The analysis population consisted of all randomized participants in Part 2 who received at least 1 dose of study intervention and were evaluable for response.	
End point type	Secondary
End point timeframe:	
Up to approximately 48 months	

### Notes:

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: There are no statistical analyses planned for this endpoint.

End point values	Part 2 First Course: Pembrolizumab+Chemotherapy+Lenvatinib	Part 2 First Course: Pembrolizumab+Chemotherapy+Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	375	373		
Units: Months				
median (full range (min-max))	1.6 (1.1 to 15.4)	1.6 (1.2 to 20.7)		



## Statistical analyses

No statistical analyses for this end point

### Secondary: Part 2: Number of Participants Who Experienced an Adverse Event (AE)

End point title	Part 2: Number of Participants Who Experienced an Adverse Event (AE) <sup>[11]</sup>
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End point description:

An adverse event is defined as any untoward medical occurrence in a clinical study participant, temporally associated with the use of study intervention, whether or not considered related to the study intervention. The number of participants who experienced one or more adverse events during Part 2 of this study were presented. The analysis population consisted of all randomized participants in Part 2 who received at least 1 dose of study intervention.

End point type	Secondary
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End point timeframe:

Up to approximately 65 months

Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: There are no statistical analyses planned for this endpoint.

End point values	Part 2 First Course: Pembrolizumab +Chemotherapy+Lenvatinib	Part 2 First Course: Pembrolizumab +Chemotherapy+Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	373	372		
Units: Participants	372	370		

## Statistical analyses

No statistical analyses for this end point

### Secondary: Part 2: Number of Participants Who Discontinued Study Drug Due to an Adverse Event

End point title	Part 2: Number of Participants Who Discontinued Study Drug Due to an Adverse Event <sup>[12]</sup>
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End point description:

An adverse event is defined as any untoward medical occurrence in a clinical study participant, temporally associated with the use of study intervention, whether or not considered related to the study intervention. The number of participants who discontinued study treatment during Part 2 of this study were presented. The analysis population consisted of all randomized participants in Part 2 who received at least 1 dose of study intervention.

End point type	Secondary
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End point timeframe:

Up to approximately 65 months

Notes:

[12] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: There are no statistical analyses planned for this endpoint.

End point values	Part 2 First Course: Pembrolizumab +Chemotherapy+Lenvatinib	Part 2 First Course: Pembrolizumab +Chemotherapy+Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	373	372		
Units: Participants	127	92		

## Statistical analyses

No statistical analyses for this end point

## Secondary: Part 2: Change from Baseline in Global Health Status (GHS) (European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30 [EORTC QLQ-C30] Items 29 and 30) Score

End point title	Part 2: Change from Baseline in Global Health Status (GHS) (European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30 [EORTC QLQ-C30] Items 29 and 30) Score <sup>[13]</sup>
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End point description:

The EORTC QLQ-C30 is a questionnaire to assess the overall quality of life of cancer patients. Participant responses to the questions regarding Global Health Status (GHS; "How would you rate your overall health during the past week?") and Quality of Life (QoL; "How would you rate your overall quality of life during the past week?") are each scored on a 7-point scale (1=Very poor to 7=Excellent). The two raw scores were averaged into a combined score, then normalized using linear transformation so each participant's score ranged from 0 to 100 (0=Worst overall health/quality of life and 100=Best overall health/quality of life). The change from baseline in GHS (EORTC QLQ-C30 Item 29) and QoL (EORTC QLQ-C30 Item 30) combined score is presented. The analysis population consisted of all randomized participants in Part 2 who received at least one dose of study treatment and have at least one EORTC-QLQ-C30 Items 29 and 30 assessment data available.

End point type	Secondary
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End point timeframe:

Baseline and Week 27

Notes:

[13] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The statistical analysis planned for part 2 first course for this endpoint.

End point values	Part 2 First Course: Pembrolizumab +Chemotherapy+Lenvatinib	Part 2 First Course: Pembrolizumab +Chemotherapy+Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	369	371		
Units: Score on a Scale				

least squares mean (confidence interval 95%)	0.65 (-1.55 to 2.84)	1.66 (-0.53 to 3.85)		
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## Statistical analyses

Statistical analysis title	Difference in Least Square Means (LS) Means
Statistical analysis description:	
Comparison based on a cLDA model with the PRO scores as the response variable with covariates for treatment by time interaction, stratification factors (baseline ECOG performance status (0 versus 1), geographic region of the enrolling site (East Asia versus non-East Asia), and baseline PD-L1 Status (<50% versus ≥50%)) as covariates.	
Comparison groups	Part 2 First Course: Pembrolizumab+Chemotherapy+Lenvatinib v Part 2 First Course: Pembrolizumab+Chemotherapy+Placebo
Number of subjects included in analysis	740
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.4805
Method	t-test, 2-sided
Parameter estimate	Difference in Least Square Means
Point estimate	-1.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.83
upper limit	1.8

## Secondary: Part 2: Change from Baseline in Cough (EORTC Quality of Life Questionnaire-Lung Cancer Module 13 [QLQ-LC13] Item 31) Score

End point title	Part 2: Change from Baseline in Cough (EORTC Quality of Life Questionnaire-Lung Cancer Module 13 [QLQ-LC13] Item 31) Score <sup>[14]</sup>
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### End point description:

The EORTC QLQ-LC13 is a lung cancer-specific supplemental questionnaire used in combination with the EORTC QLQ-C30. Participant responses to the question "How much did you cough?" are scored on a 4-point scale (1=Not at All to 4=Very Much). Using linear transformation, raw scores are standardized, so that scores range from 0 to 100. The change from baseline in cough (EORTC QLQ-LC13 Item 31) score will be presented. A lower score indicates a better outcome. The analysis population consisted of all randomized participants in Part 2 who received at least one dose of study treatment and have at least one EORTC-QLQ-C30 Item 31 assessment data available.

End point type	Secondary
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### End point timeframe:

Baseline and week 27

### Notes:

[14] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The statistical analysis planned for part 2 first course for this endpoint.

<b>End point values</b>	Part 2 First Course: Pembrolizumab +Chemotherapy +Lenvatinib	Part 2 First Course: Pembrolizumab +Chemotherapy +Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	368	371		
Units: Score on a scale				
least squares mean (confidence interval 95%)	-11.77 (-14.72 to -8.81)	-11.47 (-14.42 to -8.53)		

## Statistical analyses

<b>Statistical analysis title</b>	Difference in LS Means
Statistical analysis description:	
Comparison based on a cLDA model with the PRO scores as the response variable with covariates for treatment by time interaction, stratification factors (baseline ECOG performance status (0 versus 1), geographic region of the enrolling site (East Asia versus non-East Asia), and baseline PD-L1 Status (<50% versus ≥50%)) as covariates.	
Comparison groups	Part 2 First Course: Pembrolizumab+Chemotherapy+Lenvatinib v Part 2 First Course: Pembrolizumab+Chemotherapy+Placebo
Number of subjects included in analysis	739
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.8747
Method	t-test, 2-sided
Parameter estimate	Difference in Least Square Means
Point estimate	-0.29
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.95
upper limit	3.36

## Secondary: Part 2: Change from Baseline in Chest Pain (EORTC QLQ-LC13 Item 40) Score

End point title	Part 2: Change from Baseline in Chest Pain (EORTC QLQ-LC13 Item 40) Score <sup>[15]</sup>
End point description:	
The EORTC QLQ-LC13 is a lung cancer-specific supplemental questionnaire used in combination with the EORTC QLQ-C30. Participant responses to the question "Have you had pain in your chest?" are scored on a 4-point scale (1=Not at All to 4=Very Much). Using linear transformation, raw scores are standardized, so that scores range from 0 to 100. The change from baseline in chest pain (EORTC QLQ-LC13 Item 40) score will be presented. A lower score indicates a better outcome. The analysis population consisted of all randomized participants in Part 2 who received at least one dose of study treatment and have at least one EORTC-QLQ-C30 Item 40 assessment data available.	
End point type	Secondary
End point timeframe:	
Baseline and Week 27	

Notes:

[15] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The statistical analysis planned for part 2 first course for this endpoint.

End point values	Part 2 First Course: Pembrolizumab +Chemotherapy+Lenvatinib	Part 2 First Course: Pembrolizumab +Chemotherapy+Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	368	371		
Units: Score on a scale				
least squares mean (confidence interval 95%)	-4.61 (-7.26 to -1.96)	-3.70 (-6.34 to -1.06)		

## Statistical analyses

Statistical analysis title	Difference in LS Means
Statistical analysis description:	
Comparison based on a cLDA model with the PRO scores as the response variable with covariates for treatment by time interaction, stratification factors (baseline ECOG performance status (0 versus 1), geographic region of the enrolling site (East Asia versus non-East Asia), and baseline PD-L1 Status (<50% versus ≥50%)) as covariates.	
Comparison groups	Part 2 First Course: Pembrolizumab+Chemotherapy+Lenvatinib v Part 2 First Course: Pembrolizumab+Chemotherapy+Placebo
Number of subjects included in analysis	739
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.5941
Method	t-test, 2-sided
Parameter estimate	Difference in Least Square Means
Point estimate	-0.91
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.24
upper limit	2.43

## Secondary: Part 2: Change from Baseline in Dyspnea (EORTC QLQ-C30 Item 8) Score

End point title	Part 2: Change from Baseline in Dyspnea (EORTC QLQ-C30 Item 8) Score <sup>[16]</sup>
End point description:	
The EORTC QLQ-C30 is a questionnaire to assess the overall quality of life of cancer patients. Participant responses to the question "Were you short of breath?" are scored on a 4-point scale (1=Not at All to 4=Very Much). Using linear transformation, raw scores are standardized, so that scores range from 0 to 100. The change from baseline in dyspnea (EORTC QLQ-C30 Item 8) score will be presented. A lower score indicates a better outcome. The analysis population consisted of all randomized participants in Part 2 who received at least one dose of study treatment and have at least one EORTC-QLQ-C30 Item 8 assessment data available.	
End point type	Secondary

End point timeframe:

Baseline and Week 27

Notes:

[16] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The statistical analysis planned for part 2 first course for this endpoint.

End point values	Part 2 First Course: Pembrolizumab +Chemotherapy +Lenvatinib	Part 2 First Course: Pembrolizumab +Chemotherapy +Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	369	371		
Units: Score on a scale				
least squares mean (confidence interval 95%)	-2.77 (-6.04 to 0.50)	-0.61 (-3.86 to 2.65)		

## Statistical analyses

Statistical analysis title	Covariate
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Statistical analysis description:

Comparison based on a cLDA model with the PRO scores as the response variable with covariates for treatment by time interaction, stratification factors (baseline ECOG performance status (0 versus 1), geographic region of the enrolling site (East Asia versus non-East Asia), and baseline PD-L1 Status (<50% versus ≥50%)) as covariates.

Comparison groups	Part 2 First Course: Pembrolizumab+Chemotherapy+Lenvatinib v Part 2 First Course: Pembrolizumab+Chemotherapy+Placebo
Number of subjects included in analysis	740
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.3115
Method	t-test, 2-sided
Parameter estimate	covariate
Point estimate	-2.16
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.36
upper limit	2.03

## Secondary: Part 2: Change from Baseline in Physical Functioning (EORTC QLQ-C30 Items 1-5) Score

End point title	Part 2: Change from Baseline in Physical Functioning (EORTC QLQ-C30 Items 1-5) Score <sup>[17]</sup>
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End point description:

The EORTC QLQ-C30 is a questionnaire to assess the overall quality of life of cancer patients. Participant responses to 5 questions about their physical functioning are scored on a 4-point scale (1=Not at All to 4=Very Much). Using linear transformation, raw scores are standardized, so that scores range from 0 to 100. The change from baseline in Physical Functioning (EORTC QLQ-C30 Items 1-5) score will be presented. A higher score indicates a better quality of life. The analysis population consisted of all

randomized participants in Part 2 who received at least one dose of study treatment and have at least one EORTC-QLQ-C30 Items 1-5 assessment data available.

End point type	Secondary
End point timeframe:	
Baseline and Week 27	

Notes:

[17] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The statistical analysis planned for part 2 first course for this endpoint.

<b>End point values</b>	Part 2 First Course: Pembrolizumab + Chemotherapy + Lenvatinib	Part 2 First Course: Pembrolizumab + Chemotherapy + Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	369	371		
Units: Score on a scale				
least squares mean (confidence interval 95%)	-4.11 (-6.37 to -1.84)	-3.73 (-5.99 to -1.48)		

## Statistical analyses

<b>Statistical analysis title</b>	Covariate
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Statistical analysis description:

Comparison based on a cLDA model with the PRO scores as the response variable with covariates for treatment by time interaction, stratification factors (baseline ECOG performance status (0 versus 1), geographic region of the enrolling site (East Asia versus non-East Asia), and baseline PD-L1 Status (<50% versus ≥50%)) as covariates.

Comparison groups	Part 2 First Course: Pembrolizumab + Chemotherapy + Lenvatinib v Part 2 First Course: Pembrolizumab + Chemotherapy + Placebo
Number of subjects included in analysis	740
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.8134
Method	t-test, 2-sided
Parameter estimate	covariate
Point estimate	-0.37
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.47
upper limit	2.72

## Secondary: Part 2: Time to True Deterioration (TTD) Based on Change from Baseline in Global Health Status (GHS)/Quality of Life (QoL) (EORTC QLQ-C30 Items 29 and 30) Score

End point title	Part 2: Time to True Deterioration (TTD) Based on Change from Baseline in Global Health Status (GHS)/Quality of Life (QoL) (EORTC QLQ-C30 Items 29 and 30) Score <sup>[18]</sup>
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End point description:

TTD is defined as the time from Baseline to the first onset of a  $\geq 10$ -point negative change (decrease) from Baseline in GHS/QoL (EORTC QLQ-C30 Items 29 and 30) score. Using linear transformation, raw scores are standardized, so that scores range from 0 to 100. The TTD, as assessed based on a  $\geq 10$ -point negative change (decrease) from Baseline in GHS/QoL score, will be presented. A longer TTD indicates a better outcome. The analysis population consisted of all randomized participants in Part 2 who received at least one dose of study treatment and have at least one EORTC-QLQ-C30 Items 29 and 30 assessment data available. 9999 indicates median and upper range time to deterioration was not reached at time of data cut-off due to insufficient number of participants experiencing deterioration.

End point type	Secondary
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End point timeframe:

Baseline and Week 27

Notes:

[18] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The statistical analysis planned for part 2 first course for this endpoint.

End point values	Part 2 First Course: Pembrolizumab + Chemotherapy + Lenvatinib	Part 2 First Course: Pembrolizumab + Chemotherapy + Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	358	357		
Units: Months				
median (confidence interval 95%)	15.70 (9.66 to 9999)	9999 (21.32 to 9999)		

## Statistical analyses

Statistical analysis title	Hazard Ratio (HR)
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Statistical analysis description:

Comparison based on Cox regression model with Efron's method of tie handling with treatment as a covariate stratified by ECOG performance status (0 versus 1), geographic region of the enrolling site (East Asia versus non-East Asia), and Baseline PD-L1 Status (<50% versus  $\geq 50\%$ ).

Comparison groups	Part 2 First Course: Pembrolizumab + Chemotherapy + Lenvatinib v Part 2 First Course: Pembrolizumab + Chemotherapy + Placebo
Number of subjects included in analysis	715
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.2133
Method	Stratified Log Rank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.16
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.92
upper limit	1.47

## Secondary: Part 2: TTD Based on Change from Baseline in Cough EORTC QLQ-LC13



**(Item 31) Score**

End point title	Part 2: TTD Based on Change from Baseline in Cough EORTC QLQ-LC13 (Item 31) Score <sup>[19]</sup>
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## End point description:

TTD is defined as the time from Baseline to the first onset of a  $\geq 10$ -point negative change (decrease) from Baseline cough (EORTC QLQ-LC30 Item 31) score. Using linear transformation, raw scores are standardized, so that scores range from 0 to 100. The TTD, as assessed based on a  $\geq 10$ -point negative change (decrease) from Baseline in physical functioning score, will be presented. A longer TTD indicates a better outcome. The analysis population consisted of all randomized participants in Part 2 who received at least one dose of study treatment and have at least one EORTC-QLQ-LC30 Item 31 assessment data available at baseline. 9999 indicates median, lower and upper range time to deterioration were not reached at time of data cut-off due to insufficient number of participants experiencing deterioration.

End point type	Secondary
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## End point timeframe:

Baseline And Week 27

## Notes:

[19] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The statistical analysis planned for part 2 first course for this endpoint.

End point values	Part 2 First Course: Pembrolizumab +Chemotherapy+Lenvatinib	Part 2 First Course: Pembrolizumab +Chemotherapy+Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	356	353		
Units: Months				
median (confidence interval 95%)	9999 (9999 to 9999)	9999 (9999 to 9999)		

**Statistical analyses**

<b>Statistical analysis title</b>	Hazard Ratio (HR)
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## Statistical analysis description:

Comparison based on Cox regression model with Efron's method of tie handling with treatment as a covariate stratified by ECOG performance status (0 versus 1), geographic region of the enrolling site (East Asia versus non-East Asia), and Baseline PD-L1 Status (<50% versus  $\geq 50\%$ ).

Comparison groups	Part 2 First Course: Pembrolizumab+Chemotherapy+Lenvatinib v Part 2 First Course: Pembrolizumab+Chemotherapy+Placebo
Number of subjects included in analysis	709
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0377
Method	Stratified Log Rank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.41
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.02
upper limit	1.94

## Secondary: Part 2: TTD Based on Change from Baseline in Chest Pain EORTC QLQ-LC13 (Item 40) Score

End point title	Part 2: TTD Based on Change from Baseline in Chest Pain EORTC QLQ-LC13 (Item 40) Score <sup>[20]</sup>
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### End point description:

TTD is defined as the time from Baseline to the first onset of a  $\geq 10$ -point negative change (decrease) from Baseline chest pain (EORTC QLQ-C30 Item 40) score. Using linear transformation, raw scores are standardized, so that scores range from 0 to 100. The TTD, as assessed based on a  $\geq 10$ -point negative change (decrease) from Baseline in chest pains core, will be presented. A longer TTD indicates a better outcome. The analysis population consisted of all randomized participants in Part 2 who received at least one dose of study treatment and have at least one EORTC QLQ-LC13 chest pain Item 40 Score assessment data available at baseline. 9999 indicates median, lower and upper range time to deterioration were not reached at time of data cut-off due to insufficient number of participants experiencing deterioration.

End point type	Secondary
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### End point timeframe:

Baseline and Week 27

### Notes:

[20] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The statistical analysis planned for part 2 first course for this endpoint.

End point values	Part 2 First Course: Pembrolizumab +Chemotherapy+Lenvatinib	Part 2 First Course: Pembrolizumab +Chemotherapy+Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	356	353		
Units: Months				
median (confidence interval 95%)	9999 (9999 to 9999)	9999 (9999 to 9999)		

## Statistical analyses

Statistical analysis title	Hazard Ratio (HR)
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### Statistical analysis description:

Comparison based on Cox regression model with Efron's method of tie handling with treatment as a covariate stratified by ECOG performance status (0 versus 1), geographic region of the enrolling site (East Asia versus non-East Asia), and Baseline PD-L1 Status (<50% versus  $\geq 50\%$ ).

Comparison groups	Part 2 First Course: Pembrolizumab+Chemotherapy+Lenvatinib v Part 2 First Course: Pembrolizumab+Chemotherapy+Placebo
Number of subjects included in analysis	709
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.4084
Method	Stratified Log Rank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.87

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.62
upper limit	1.21

## Secondary: Part 2: TTD Based on Change from Baseline in Dyspnea EORTC QLQ-C30 (Item 8) Score

End point title	Part 2: TTD Based on Change from Baseline in Dyspnea EORTC QLQ-C30 (Item 8) Score <sup>[21]</sup>
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End point description:

TTD is defined as the time from Baseline to the first onset of a  $\geq 10$ -point negative change (decrease) from Baseline dyspnea (EORTC QLQ-C30 Item 8) score. Using linear transformation, raw scores are standardized, so that scores range from 0 to 100. The TTD, as assessed based on a  $\geq 10$ -point negative change (decrease) from Baseline in dyspnea score, will be presented. A longer TTD indicates a better outcome. The analysis population consisted of all randomized participants in Part 2 who received at least one dose of study treatment and have at least one EORTC-QLQ-C30 Item 8 assessment data available at baseline. 9999 indicates median, lower and upper range time to deterioration were not reached at time of data cut-off due to insufficient number of participants experiencing deterioration.

End point type	Secondary
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End point timeframe:

Baseline and Week 27

Notes:

[21] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The statistical analysis planned for part 2 first course for this endpoint.

<b>End point values</b>	Part 2 First Course: Pembrolizumab + Chemotherapy + Lenvatinib	Part 2 First Course: Pembrolizumab + Chemotherapy + Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	358	357		
Units: Months				
median (confidence interval 95%)	9999 (9999 to 9999)	9999 (9999 to 9999)		

## Statistical analyses

<b>Statistical analysis title</b>	Hazard Ratio (HR)
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Statistical analysis description:

Comparison based on Cox regression model with Efron's method of tie handling with treatment as a covariate stratified by ECOG performance status (0 versus 1), geographic region of the enrolling site (East Asia versus non-East Asia), and Baseline PD-L1 Status (<50% versus  $\geq 50\%$ ).

Comparison groups	Part 2 First Course: Pembrolizumab + Chemotherapy + Lenvatinib v Part 2 First Course: Pembrolizumab + Chemotherapy + Placebo
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Number of subjects included in analysis	715
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.7955
Method	Stratified Log Rank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.79
upper limit	1.36

## Secondary: Part 2: TTD Based on Change from Baseline in Physical Functioning EORTC QLQ-C30 (Items 1 through 5) Score

End point title	Part 2: TTD Based on Change from Baseline in Physical Functioning EORTC QLQ-C30 (Items 1 through 5) Score <sup>[22]</sup>
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End point description:

TTD is defined as the time from Baseline to the first onset of a  $\geq 10$ -point negative change (decrease) from Baseline physical functioning (EORTC QLQ-C30 Items 1 through 5) score. Using linear transformation, raw scores are standardized, so that scores range from 0 to 100. The TTD, as assessed based on a  $\geq 10$ -point negative change (decrease) from Baseline in physical functioning score, will be presented. A longer TTD indicates a better outcome. The analysis population consisted of all randomized participants in Part 2 who received at least one dose of study treatment and have at least one EORTC-QLQ-C30 Items 1 through 5 assessment data available at baseline. 9999 indicates median, lower and upper range time to deterioration were not reached at time of data cut-off due to insufficient number of participants experiencing deterioration.

End point type	Secondary
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End point timeframe:

Baseline and Week 27

Notes:

[22] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The statistical analysis planned for part 2 first course for this endpoint.

End point values	Part 2 First Course: Pembrolizumab +Chemotherapy+Lenvatinib	Part 2 First Course: Pembrolizumab +Chemotherapy+Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	358	357		
Units: Months				
median (confidence interval 95%)	16.82 (8.84 to 22.51)	9999 (9999 to 9999)		

## Statistical analyses

No statistical analyses for this end point

## Secondary: Part 2: Time to True Deterioration (TTD) Based on Change from Baseline in the Composite Endpoint of Cough (EORTC QLQ-LC13 Item 31), Chest Pain (EORTC QLQ-LC13 Item 40), or Dyspnea (EORTC QLQ-C30 Item 8)

End point title	Part 2: Time to True Deterioration (TTD) Based on Change from Baseline in the Composite Endpoint of Cough (EORTC QLQ-LC13 Item 31), Chest Pain (EORTC QLQ-LC13 Item 40), or Dyspnea (EORTC QLQ-C30 Item 8) <sup>[23]</sup>
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### End point description:

TTD is defined as the time from Baseline to the first onset of a  $\geq 10$ -point negative change (decrease) from Baseline in the composite endpoint of cough (QLQ-LC13 item 31), chest pain (QLQ-LC13 item 40), or dyspnea (QLQ-C30 Item 8). Using linear transformation, raw scores are standardized, so that scores range from 0 to 100. The TTD, as assessed based on a  $\geq 10$ -point negative change (decrease) from Baseline in the composite endpoint of cough, chest pain or dyspnea, will be presented. A longer TTD indicates a better outcome. The analysis population consisted of all randomized participants in Part 2 who received at least one dose of study treatment and have at least one EORTC-QLQ-LC13 Items 31 and 40 and EORTC-QLQ-C30 Item 8 assessment data available.

End point type	Secondary
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### End point timeframe:

Baseline and Week 27

### Notes:

[23] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The statistical analysis planned for part 2 first course for this endpoint.

End point values	Part 2 First Course: Pembrolizumab +Chemotherapy +Lenvatinib	Part 2 First Course: Pembrolizumab +Chemotherapy +Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	358	358		
Units: Months				
median (confidence interval 95%)	8.28 (5.98 to 11.07)	9.33 (7.03 to 12.91)		

## Statistical analyses

Statistical analysis title	Hazard Ratio (HR)
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### Statistical analysis description:

Comparison based on Cox regression model with Efron's method of tie handling with treatment as a covariate stratified by ECOG performance status (0 versus 1), geographic region of the enrolling site (East Asia versus non-East Asia), and Baseline PD-L1 Status (<50% versus  $\geq 50\%$ ).

Comparison groups	Part 2 First Course: Pembrolizumab+Chemotherapy+Lenvatinib v Part 2 First Course: Pembrolizumab+Chemotherapy+Placebo
Number of subjects included in analysis	716
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.7191
Method	Stratified Log Rank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.04

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.84
upper limit	1.28

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Up to approximately 58 months

Adverse event reporting additional description:

All-cause mortality was reported on all randomized participants (first and second course). Serious and non-serious AEs were reported among participants who received at least one dose of study treatment. MedDRA preferred terms 'Neoplasm progression', 'Malignant neoplasm progression' and 'Disease progression' not related to the drug were excluded.

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	26.0
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### Reporting groups

Reporting group title	Part 1 First Course: Pembrolizumab+Chemotherapy+Lenvatinib
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Reporting group description:

Participants received carboplatin AUC5 or cisplatin 75 mg/m<sup>2</sup> via IV infusion Q3W for 4 cycles PLUS pemetrexed 500 mg/m<sup>2</sup> via IV infusion Q3W for 4 cycles PLUS pembrolizumab 200 mg via IV infusion Q3W for up to 35 cycles (up to 2 years) PLUS lenvatinib 8 mg via oral capsule once daily.

Reporting group title	Part 2 First Course: Pembrolizumab+Chemotherapy+Lenvatinib
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Reporting group description:

Participants received carboplatin Area Under Curve 5 mg/mL/min (AUC5) or cisplatin 75 mg/m<sup>2</sup> via intravenous (IV) infusion on Day 1 of each 3-week cycle (Q3W) for 4 cycles PLUS pemetrexed 500 mg/m<sup>2</sup> via IV infusion Q3W for 4 cycles PLUS pembrolizumab 200 mg via IV infusion Q3W for up to 35 cycles (up to 2 years) PLUS lenvatinib 8 mg via oral capsule once daily.

Reporting group title	Part 2 Second Course: Pembrolizumab+Chemotherapy+Lenvatinib
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Reporting group description:

Qualified participants who completed the first course of pembrolizumab plus chemotherapy plus lenvatinib for up to 35 cycles (up to 2 years), but experienced disease progression, initiated a second course of pembrolizumab at the investigator's discretion, at 200 mg IV Q2W for up to ~1 year. Participants previously receiving Lenvatinib could continue receiving lenvatinib at investigator's discretion.

Reporting group title	Part1 Second Course:Pembrolizumab OnlyChemotherapy+Lenvatinib
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Reporting group description:

Qualified participants who completed the first course of pembrolizumab plus chemotherapy plus lenvatinib for up to 35 cycles (up to 2 years), but experienced disease progression, initiated a second course of pembrolizumab at the investigator's discretion, at 200 mg IV Q2W for up to ~1 year, without chemotherapy plus lenvatinib.

Reporting group title	Part 2 Second Course: Pembrolizumab+Chemotherapy+Placebo
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Reporting group description:

Qualified participants who completed the first course of pembrolizumab plus chemotherapy plus lenvatinib for up to 35 cycles (up to 2 years), but experienced disease progression, initiated a second course of pembrolizumab at the investigator's discretion, at 200 mg IV Q2W for up to ~1 year. Participants previously receiving Lenvatinib could continue receiving lenvatinib at investigator's discretion.

Reporting group title	Part 2 First Course: Pembrolizumab+Chemotherapy+Placebo
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Reporting group description:

Participants received carboplatin AUC5 or cisplatin 75 mg/m<sup>2</sup> via IV infusion Q3W for 4 cycles PLUS pemetrexed 500 mg/m<sup>2</sup> via IV infusion Q3W for 4 cycles PLUS pembrolizumab 200 mg via IV infusion Q3W for up to 35 cycles (up to 2 years) PLUS placebo matching lenvatinib via oral capsule once daily.

<b>Serious adverse events</b>	Part 1 First Course: Pembrolizumab+Chemotherapy+Lenvatinib	Part 2 First Course: Pembrolizumab+Chemotherapy+Lenvatinib	Part 2 Second Course: Pembrolizumab+Chemotherapy+Lenvatinib
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 13 (53.85%)	232 / 373 (62.20%)	1 / 3 (33.33%)
number of deaths (all causes)	9	278	3
number of deaths resulting from adverse events	3	57	1
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer metastatic			
subjects affected / exposed	0 / 13 (0.00%)	0 / 373 (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
Cancer pain			
subjects affected / exposed	0 / 13 (0.00%)	2 / 373 (0.54%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Invasive ductal breast carcinoma			
subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	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
Liposarcoma			
subjects affected / exposed	0 / 13 (0.00%)	0 / 373 (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
Metastases to central nervous system			
subjects affected / exposed	0 / 13 (0.00%)	0 / 373 (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
Neoplasm malignant			
subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	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 / 1	0 / 0
Tumour associated fever			



subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	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
Tumour pain			
subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	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
Vascular disorders			
Aortic aneurysm			
subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	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
Arterial disorder			
subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arterial thrombosis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 373 (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
Hypotension			
subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	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
Hypertension			
subjects affected / exposed	0 / 13 (0.00%)	2 / 373 (0.54%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Embolism			
subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Deep vein thrombosis			

subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Superior vena cava syndrome			
subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	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 artery thrombosis			
subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral arterial occlusive disease			
subjects affected / exposed	0 / 13 (0.00%)	0 / 373 (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
Jugular vein thrombosis			
subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	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
Venous thrombosis limb			
subjects affected / exposed	0 / 13 (0.00%)	0 / 373 (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
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 13 (0.00%)	4 / 373 (1.07%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chest discomfort			
subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	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
General physical health deterioration			

subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Death			
subjects affected / exposed	0 / 13 (0.00%)	10 / 373 (2.68%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 10	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 10	0 / 0
Fatigue			
subjects affected / exposed	0 / 13 (0.00%)	2 / 373 (0.54%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chest pain			
subjects affected / exposed	0 / 13 (0.00%)	0 / 373 (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
Malaise			
subjects affected / exposed	0 / 13 (0.00%)	2 / 373 (0.54%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mucosal inflammation			
subjects affected / exposed	0 / 13 (0.00%)	2 / 373 (0.54%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oedema			
subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	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
Non-cardiac chest pain			
subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	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
Multiple organ dysfunction syndrome			

subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	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 / 1	0 / 0
Pain			
subjects affected / exposed	1 / 13 (7.69%)	0 / 373 (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
Peripheral swelling			
subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	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
Sudden death			
subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	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 / 1	0 / 0
Pyrexia			
subjects affected / exposed	1 / 13 (7.69%)	5 / 373 (1.34%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 5	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Anaphylactic shock			
subjects affected / exposed	0 / 13 (0.00%)	2 / 373 (0.54%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anaphylactic reaction			
subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	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
Reproductive system and breast disorders			
Benign prostatic hyperplasia			
subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	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

Prostatitis			
subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 13 (0.00%)	3 / 373 (0.80%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Emphysema			
subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	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
Acute respiratory failure			
subjects affected / exposed	0 / 13 (0.00%)	2 / 373 (0.54%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 2	0 / 0
Bronchopneumopathy			
subjects affected / exposed	0 / 13 (0.00%)	0 / 373 (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	0 / 13 (0.00%)	1 / 373 (0.27%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pharyngeal haemorrhage			
subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	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
Lung infiltration			
subjects affected / exposed	0 / 13 (0.00%)	0 / 373 (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

Interstitial lung disease			
subjects affected / exposed	0 / 13 (0.00%)	3 / 373 (0.80%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	3 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Immune-mediated lung disease			
subjects affected / exposed	0 / 13 (0.00%)	5 / 373 (1.34%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	5 / 5	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hydrothorax			
subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	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
Haemoptysis			
subjects affected / exposed	1 / 13 (7.69%)	4 / 373 (1.07%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	2 / 5	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 0
Pleural effusion			
subjects affected / exposed	1 / 13 (7.69%)	10 / 373 (2.68%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	3 / 10	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epistaxis			
subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	3 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary artery thrombosis			
subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumothorax spontaneous			
subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumothorax			

subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	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
Pneumonitis			
subjects affected / exposed	1 / 13 (7.69%)	14 / 373 (3.75%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	1 / 1	12 / 14	0 / 0
deaths causally related to treatment / all	0 / 0	5 / 5	0 / 0
Pleurisy			
subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	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
Pulmonary embolism			
subjects affected / exposed	0 / 13 (0.00%)	11 / 373 (2.95%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	6 / 11	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary fibrosis			
subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	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 / 1	0 / 0
Pulmonary infarction			
subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory arrest			
subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	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 / 1	0 / 0
Respiratory failure			
subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	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
Psychiatric disorders			
Behaviour disorder			

subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	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
Completed suicide			
subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	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 / 1	0 / 0
Suicidal ideation			
subjects affected / exposed	0 / 13 (0.00%)	0 / 373 (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
Disorientation			
subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	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
Delirium			
subjects affected / exposed	0 / 13 (0.00%)	2 / 373 (0.54%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Confusional state			
subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicide attempt			
subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	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
Product issues			
Device dislocation			
subjects affected / exposed	0 / 13 (0.00%)	0 / 373 (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
Investigations			



Aspartate aminotransferase increased			
subjects affected / exposed	0 / 13 (0.00%)	3 / 373 (0.80%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	3 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Amylase increased			
subjects affected / exposed	0 / 13 (0.00%)	0 / 373 (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
Alanine aminotransferase increased			
subjects affected / exposed	0 / 13 (0.00%)	3 / 373 (0.80%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	3 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lipase increased			
subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 13 (0.00%)	2 / 373 (0.54%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood creatinine increased			
subjects affected / exposed	0 / 13 (0.00%)	3 / 373 (0.80%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	3 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymphocyte count decreased			
subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutrophil count decreased			
subjects affected / exposed	1 / 13 (7.69%)	3 / 373 (0.80%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	1 / 1	2 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Platelet count decreased			

subjects affected / exposed	0 / 13 (0.00%)	10 / 373 (2.68%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	10 / 10	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SARS-CoV-2 test positive			
subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	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 / 1	0 / 0
Weight decreased			
subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
White blood cell count decreased			
subjects affected / exposed	1 / 13 (7.69%)	2 / 373 (0.54%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	1 / 1	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Femur fracture			
subjects affected / exposed	0 / 13 (0.00%)	0 / 373 (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
Fall			
subjects affected / exposed	0 / 13 (0.00%)	0 / 373 (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
Craniocerebral injury			
subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	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
Fracture			
subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	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
Hip fracture			

subjects affected / exposed	0 / 13 (0.00%)	0 / 373 (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
Joint dislocation			
subjects affected / exposed	0 / 13 (0.00%)	0 / 373 (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
Procedural pain			
subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	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
Procedural pneumothorax			
subjects affected / exposed	0 / 13 (0.00%)	0 / 373 (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
Foot fracture			
subjects affected / exposed	0 / 13 (0.00%)	0 / 373 (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
Subdural haematoma			
subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	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
Tracheal haemorrhage			
subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Toxicity to various agents			
subjects affected / exposed	1 / 13 (7.69%)	0 / 373 (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
Tendon rupture			

subjects affected / exposed	0 / 13 (0.00%)	0 / 373 (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
Synovial rupture			
subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	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
Cardiac disorders			
Acute coronary syndrome			
subjects affected / exposed	0 / 13 (0.00%)	2 / 373 (0.54%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute myocardial infarction			
subjects affected / exposed	0 / 13 (0.00%)	0 / 373 (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
Arteriosclerosis coronary artery			
subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	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
Angina pectoris			
subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	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
Atrial fibrillation			
subjects affected / exposed	1 / 13 (7.69%)	2 / 373 (0.54%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial flutter			
subjects affected / exposed	0 / 13 (0.00%)	0 / 373 (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
Atrial thrombosis			

subjects affected / exposed	0 / 13 (0.00%)	0 / 373 (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 failure congestive			
subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac arrest			
subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 1
Cardiac tamponade			
subjects affected / exposed	0 / 13 (0.00%)	0 / 373 (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
Cardio-respiratory arrest			
subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Coronary artery disease			
subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	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
Immune-mediated myocarditis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 373 (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	0 / 13 (0.00%)	6 / 373 (1.61%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	4 / 6	0 / 0
deaths causally related to treatment / all	0 / 0	2 / 3	0 / 0
Myocarditis			

subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Pericardial effusion			
subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	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 / 1	0 / 0
Sinus tachycardia			
subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	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
Nervous system disorders			
Brain oedema			
subjects affected / exposed	0 / 13 (0.00%)	0 / 373 (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 ganglia infarction			
subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	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
Cerebral haemorrhage			
subjects affected / exposed	0 / 13 (0.00%)	0 / 373 (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
Dysarthria			
subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	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
Cognitive disorder			
subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrovascular accident			

subjects affected / exposed	0 / 13 (0.00%)	5 / 373 (1.34%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	3 / 5	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Cerebral thrombosis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 373 (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 ischaemia			
subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	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
Cerebral infarction			
subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Encephalopathy			
subjects affected / exposed	0 / 13 (0.00%)	2 / 373 (0.54%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Lethargy			
subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic stroke			
subjects affected / exposed	0 / 13 (0.00%)	2 / 373 (0.54%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic cerebral infarction			
subjects affected / exposed	0 / 13 (0.00%)	0 / 373 (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
Intracranial aneurysm			

subjects affected / exposed	0 / 13 (0.00%)	0 / 373 (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
Immune-mediated encephalopathy			
subjects affected / exposed	0 / 13 (0.00%)	0 / 373 (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
Haemorrhagic stroke			
subjects affected / exposed	0 / 13 (0.00%)	0 / 373 (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
Epilepsy			
subjects affected / exposed	0 / 13 (0.00%)	2 / 373 (0.54%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seizure			
subjects affected / exposed	0 / 13 (0.00%)	3 / 373 (0.80%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spondylitic myelopathy			
subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	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
Spinal cord compression			
subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	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
Sensory disturbance			



subjects affected / exposed	0 / 13 (0.00%)	0 / 373 (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
<b>Blood and lymphatic system disorders</b>			
<b>Anaemia</b>			
subjects affected / exposed	1 / 13 (7.69%)	17 / 373 (4.56%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	1 / 1	16 / 19	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>Febrile neutropenia</b>			
subjects affected / exposed	0 / 13 (0.00%)	12 / 373 (3.22%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	13 / 13	0 / 0
deaths causally related to treatment / all	0 / 0	3 / 3	0 / 0
<b>Bone marrow failure</b>			
subjects affected / exposed	0 / 13 (0.00%)	0 / 373 (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
<b>Neutropenia</b>			
subjects affected / exposed	0 / 13 (0.00%)	4 / 373 (1.07%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 5	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>Spontaneous haematoma</b>			
subjects affected / exposed	0 / 13 (0.00%)	0 / 373 (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
<b>Thrombocytopenia</b>			
subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>Ear and labyrinth disorders</b>			
<b>Vertigo</b>			
subjects affected / exposed	0 / 13 (0.00%)	0 / 373 (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
<b>Vertigo positional</b>			

subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	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
Eye disorders			
Retinal detachment			
subjects affected / exposed	0 / 13 (0.00%)	0 / 373 (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
Cataract			
subjects affected / exposed	0 / 13 (0.00%)	0 / 373 (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
Ulcerative keratitis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 373 (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
Vitreous haemorrhage			
subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	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
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	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
Coeliac artery stenosis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 373 (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
Anal fistula			
subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	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
Ascites			

subjects affected / exposed	0 / 13 (0.00%)	0 / 373 (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
Abdominal pain upper			
subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	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
Colitis			
subjects affected / exposed	1 / 13 (7.69%)	2 / 373 (0.54%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Constipation			
subjects affected / exposed	1 / 13 (7.69%)	1 / 373 (0.27%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dysphagia			
subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	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
Duodenitis			
subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	0 / 13 (0.00%)	7 / 373 (1.88%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	7 / 9	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enteritis			
subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	3 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Faecaloma			

subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	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
Gastric ulcer haemorrhage			
subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematochezia			
subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 13 (0.00%)	2 / 373 (0.54%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal inflammation			
subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	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
Gastritis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 373 (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
Ileus			
subjects affected / exposed	0 / 13 (0.00%)	0 / 373 (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
Immune-mediated enterocolitis			

subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Inguinal hernia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 373 (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
Oral pain			
subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	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
Neutropenic colitis			
subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	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
Obstruction gastric			
subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal perforation			
subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	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 / 1	0 / 0
Pancreatitis			
subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis acute			

subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper gastrointestinal haemorrhage			
subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stomatitis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 373 (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
Subileus			
subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	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
Proctitis			
subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	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
Vomiting			
subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	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
Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	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
Cholecystitis			
subjects affected / exposed	0 / 13 (0.00%)	3 / 373 (0.80%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholelithiasis			

subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	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
Hepatic cirrhosis			
subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	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
Hepatic haematoma			
subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	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
Hepatic failure			
subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Hepatic cytolysis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 373 (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
Hepatitis			
subjects affected / exposed	1 / 13 (7.69%)	3 / 373 (0.80%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	3 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune-mediated hepatitis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 373 (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
Perforation bile duct			
subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	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
Skin and subcutaneous tissue disorders			
Dermatitis herpetiformis			

subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pseudocellulitis			
subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rash			
subjects affected / exposed	0 / 13 (0.00%)	2 / 373 (0.54%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Superficial inflammatory dermatosis			
subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Immune-mediated nephritis			
subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Autoimmune nephritis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 373 (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 kidney injury			
subjects affected / exposed	1 / 13 (7.69%)	6 / 373 (1.61%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	1 / 1	4 / 7	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Nephritis			
subjects affected / exposed	0 / 13 (0.00%)	2 / 373 (0.54%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nephropathy			



subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Proteinuria			
subjects affected / exposed	0 / 13 (0.00%)	0 / 373 (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 failure			
subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract obstruction			
subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	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
Tubulointerstitial nephritis			
subjects affected / exposed	0 / 13 (0.00%)	2 / 373 (0.54%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal impairment			
subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
Adrenal haematoma			
subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Adrenal insufficiency			
subjects affected / exposed	1 / 13 (7.69%)	3 / 373 (0.80%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	1 / 1	3 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperthyroidism			

subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypophysitis			
subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypothyroidism			
subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	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
Musculoskeletal and connective tissue disorders			
Myositis			
subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Muscular weakness			
subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	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
Back pain			
subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	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
Arthralgia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 373 (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			
subjects affected / exposed	0 / 13 (0.00%)	0 / 373 (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	0 / 13 (0.00%)	1 / 373 (0.27%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pathological fracture			
subjects affected / exposed	0 / 13 (0.00%)	2 / 373 (0.54%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rotator cuff syndrome			
subjects affected / exposed	0 / 13 (0.00%)	0 / 373 (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
Infections and infestations			
Anorectal infection			
subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	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
Abdominal sepsis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 373 (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
Appendicitis			
subjects affected / exposed	0 / 13 (0.00%)	2 / 373 (0.54%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Biliary sepsis			
subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	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 / 1	0 / 0
Bronchitis			
subjects affected / exposed	1 / 13 (7.69%)	2 / 373 (0.54%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Catheter site infection			

subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	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
COVID-19			
subjects affected / exposed	0 / 13 (0.00%)	7 / 373 (1.88%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 7	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 2	0 / 0
COVID-19 pneumonia			
subjects affected / exposed	0 / 13 (0.00%)	5 / 373 (1.34%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 5	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 3	0 / 0
Campylobacter gastroenteritis			
subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	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
Bronchitis viral			
subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	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
Cellulitis			
subjects affected / exposed	0 / 13 (0.00%)	2 / 373 (0.54%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium difficile colitis			
subjects affected / exposed	0 / 13 (0.00%)	2 / 373 (0.54%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Erysipelas			
subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Encephalitis			

subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis			
subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile infection			
subjects affected / exposed	0 / 13 (0.00%)	0 / 373 (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
Gastroenteritis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 373 (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
Herpes zoster			
subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infection			
subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	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
Lower respiratory tract infection			
subjects affected / exposed	0 / 13 (0.00%)	4 / 373 (1.07%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myelitis			
subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenic sepsis			

subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	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
Osteomyelitis			
subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Parainfluenzae virus infection			
subjects affected / exposed	0 / 13 (0.00%)	0 / 373 (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
Peritonsillar abscess			
subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	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
Pneumocystis jirovecii pneumonia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 373 (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			
subjects affected / exposed	2 / 13 (15.38%)	28 / 373 (7.51%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	3 / 3	13 / 37	0 / 0
deaths causally related to treatment / all	0 / 0	3 / 7	0 / 0
Pneumonia aspiration			
subjects affected / exposed	0 / 13 (0.00%)	3 / 373 (0.80%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Pneumonia bacterial			
subjects affected / exposed	0 / 13 (0.00%)	2 / 373 (0.54%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Pneumonia fungal			

subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia klebsiella			
subjects affected / exposed	0 / 13 (0.00%)	0 / 373 (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 sepsis			
subjects affected / exposed	0 / 13 (0.00%)	0 / 373 (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
Pyelonephritis			
subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis acute			
subjects affected / exposed	0 / 13 (0.00%)	0 / 373 (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 tract infection			
subjects affected / exposed	0 / 13 (0.00%)	4 / 373 (1.07%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Sepsis			
subjects affected / exposed	0 / 13 (0.00%)	7 / 373 (1.88%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 7	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 2	0 / 0
Septic shock			
subjects affected / exposed	1 / 13 (7.69%)	1 / 373 (0.27%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Sinusitis			

subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	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
Urinary tract infection			
subjects affected / exposed	0 / 13 (0.00%)	0 / 373 (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
Tuberculosis			
subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Soft tissue infection			
subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	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
Skin infection			
subjects affected / exposed	0 / 13 (0.00%)	2 / 373 (0.54%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Varicella zoster virus infection			
subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	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
Urosepsis			
subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	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
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	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
Decreased appetite			



subjects affected / exposed	0 / 13 (0.00%)	2 / 373 (0.54%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetic ketoacidosis			
subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperkalaemia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 373 (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
Hyperglycaemia			
subjects affected / exposed	0 / 13 (0.00%)	0 / 373 (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
Electrolyte imbalance			
subjects affected / exposed	0 / 13 (0.00%)	0 / 373 (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
Hypokalaemia			
subjects affected / exposed	0 / 13 (0.00%)	2 / 373 (0.54%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemia			
subjects affected / exposed	0 / 13 (0.00%)	3 / 373 (0.80%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Type 2 diabetes mellitus			
subjects affected / exposed	0 / 13 (0.00%)	2 / 373 (0.54%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

<b>Serious adverse events</b>	Part1 Second Course:Pembrolizumab	Part 2 Second Course: Pembrolizumab+Che	Part 2 First Course: Pembrolizumab+Chemotherapy+Placebo
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	Only Chemotherapy+ Lenvatinib	Chemotherapy+Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 1 (100.00%)	3 / 7 (42.86%)	189 / 372 (50.81%)
number of deaths (all causes)	0	3	266
number of deaths resulting from adverse events	0	1	44
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer metastatic			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	1 / 372 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cancer pain			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	1 / 372 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Invasive ductal breast carcinoma			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Liposarcoma			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	1 / 372 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metastases to central nervous system			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	1 / 372 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Neoplasm malignant			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
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 associated fever			

subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
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	0 / 1 (0.00%)	0 / 7 (0.00%)	1 / 372 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Aortic aneurysm			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arterial disorder			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arterial thrombosis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	1 / 372 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypotension			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	2 / 372 (0.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertension			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Embolism			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Deep vein thrombosis			

subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	4 / 372 (1.08%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Superior vena cava syndrome			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral artery thrombosis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral arterial occlusive disease			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	1 / 372 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Jugular vein thrombosis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Venous thrombosis limb			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	1 / 372 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	2 / 372 (0.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chest discomfort			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General physical health deterioration			

subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Death			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	5 / 372 (1.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	2 / 5
Fatigue			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	2 / 372 (0.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chest pain			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	1 / 372 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malaise			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mucosal inflammation			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oedema			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Non-cardiac chest pain			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Multiple organ dysfunction syndrome			

subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral swelling			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sudden death			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	3 / 372 (0.81%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Anaphylactic shock			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anaphylactic reaction			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
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			
Benign prostatic hyperplasia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Prostatitis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
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			
Dyspnoea			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	1 / 372 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Emphysema			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
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 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchopneumopathy			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	1 / 372 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	2 / 372 (0.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pharyngeal haemorrhage			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung infiltration			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	1 / 372 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Interstitial lung disease			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	4 / 372 (1.08%)
occurrences causally related to treatment / all	0 / 0	0 / 0	4 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune-mediated lung disease			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	2 / 372 (0.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hydrothorax			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	1 / 372 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemoptysis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	2 / 372 (0.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Pleural effusion			
subjects affected / exposed	0 / 1 (0.00%)	1 / 7 (14.29%)	9 / 372 (2.42%)
occurrences causally related to treatment / all	0 / 0	0 / 1	1 / 10
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Epistaxis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
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 artery thrombosis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumothorax spontaneous			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumothorax			



subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	2 / 372 (0.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonitis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	15 / 372 (4.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	15 / 16
deaths causally related to treatment / all	0 / 0	0 / 0	2 / 2
Pleurisy			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	1 / 372 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	0 / 1 (0.00%)	1 / 7 (14.29%)	8 / 372 (2.15%)
occurrences causally related to treatment / all	0 / 0	0 / 1	4 / 8
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 3
Pulmonary fibrosis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
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 infarction			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
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 arrest			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	1 / 372 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Psychiatric disorders			
Behaviour disorder			

subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Completed suicide			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicidal ideation			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	1 / 372 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Disorientation			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Delirium			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	1 / 372 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Confusional state			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	1 / 372 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicide attempt			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
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 dislocation			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	1 / 372 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			

Aspartate aminotransferase increased			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	5 / 372 (1.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	4 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Amylase increased			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	1 / 372 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Alanine aminotransferase increased			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	7 / 372 (1.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	6 / 7
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lipase increased			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	1 / 372 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood creatinine increased			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	1 / 372 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymphocyte count decreased			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutrophil count decreased			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	6 / 372 (1.61%)
occurrences causally related to treatment / all	0 / 0	0 / 0	6 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Platelet count decreased			

subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	8 / 372 (2.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	7 / 8
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SARS-CoV-2 test positive			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Weight decreased			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
White blood cell count decreased			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	4 / 372 (1.08%)
occurrences causally related to treatment / all	0 / 0	0 / 0	4 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Femur fracture			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	1 / 372 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fall			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	1 / 372 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Craniocerebral injury			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fracture			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hip fracture			

subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	1 / 372 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Joint dislocation			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	1 / 372 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Procedural pain			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Procedural pneumothorax			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	1 / 372 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Foot fracture			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	1 / 372 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subdural haematoma			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tracheal haemorrhage			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Toxicity to various agents			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tendon rupture			

subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	1 / 372 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Synovial rupture			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
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			
Acute coronary syndrome			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	2 / 372 (0.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Acute myocardial infarction			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	1 / 372 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Arteriosclerosis coronary artery			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina pectoris			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial fibrillation			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	2 / 372 (0.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial flutter			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	1 / 372 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial thrombosis			

subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	1 / 372 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure congestive			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
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	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
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 tamponade			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	1 / 372 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardio-respiratory arrest			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	1 / 372 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Coronary artery disease			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune-mediated myocarditis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	1 / 372 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	1 / 372 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocarditis			

subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pericardial effusion			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	2 / 372 (0.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinus tachycardia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Brain oedema			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	1 / 372 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Basal ganglia infarction			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
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	0 / 1 (0.00%)	0 / 7 (0.00%)	2 / 372 (0.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 2
Dysarthria			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cognitive disorder			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
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	0 / 1 (0.00%)	0 / 7 (0.00%)	4 / 372 (1.08%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral thrombosis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	1 / 372 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral ischaemia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	1 / 372 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Cerebral infarction			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	1 / 372 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Encephalopathy			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	1 / 372 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lethargy			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic stroke			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	2 / 372 (0.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Ischaemic cerebral infarction			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	1 / 372 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Intracranial aneurysm			

subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	1 / 372 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune-mediated encephalopathy			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	1 / 372 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhagic stroke			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	1 / 372 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epilepsy			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seizure			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	1 / 372 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spondylitic myelopathy			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal cord compression			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	2 / 372 (0.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sensory disturbance			

subjects affected / exposed	0 / 1 (0.00%)	1 / 7 (14.29%)	0 / 372 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
<b>Blood and lymphatic system disorders</b>			
<b>Anaemia</b>			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	9 / 372 (2.42%)
occurrences causally related to treatment / all	0 / 0	0 / 0	7 / 9
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>Febrile neutropenia</b>			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	5 / 372 (1.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	5 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>Bone marrow failure</b>			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	1 / 372 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>Neutropenia</b>			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>Spontaneous haematoma</b>			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	1 / 372 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>Thrombocytopenia</b>			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>Ear and labyrinth disorders</b>			
<b>Vertigo</b>			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	1 / 372 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>Vertigo positional</b>			

subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Retinal detachment			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	1 / 372 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cataract			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	2 / 372 (0.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ulcerative keratitis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	1 / 372 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vitreous haemorrhage			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	1 / 372 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coeliac artery stenosis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	1 / 372 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anal fistula			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ascites			

subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	2 / 372 (0.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain upper			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	5 / 372 (1.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	3 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Constipation			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	1 / 372 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dysphagia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Duodenitis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
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	0 / 1 (0.00%)	0 / 7 (0.00%)	4 / 372 (1.08%)
occurrences causally related to treatment / all	0 / 0	0 / 0	4 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enteritis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	1 / 372 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Faecaloma			

subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric ulcer haemorrhage			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematochezia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal inflammation			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastritis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	2 / 372 (0.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ileus			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	1 / 372 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune-mediated enterocolitis			

subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	1 / 372 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Inguinal hernia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	1 / 372 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oral pain			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	5 / 372 (1.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	4 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenic colitis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Obstruction gastric			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal perforation			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	2 / 372 (0.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis acute			

subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper gastrointestinal haemorrhage			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	2 / 372 (0.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Stomatitis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	1 / 372 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subileus			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Proctitis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	4 / 372 (1.08%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	1 / 372 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholelithiasis			



subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic cirrhosis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic haematoma			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic failure			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic cytolysis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	1 / 372 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatitis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune-mediated hepatitis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	2 / 372 (0.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Perforation bile duct			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
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 herpetiformis			

subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pseudocellulitis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	1 / 372 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rash			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	1 / 372 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Superficial inflammatory dermatosis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Immune-mediated nephritis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Autoimmune nephritis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	1 / 372 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute kidney injury			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	3 / 372 (0.81%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nephritis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	1 / 372 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nephropathy			

subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Proteinuria			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	1 / 372 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal failure			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	2 / 372 (0.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Urinary tract obstruction			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tubulointerstitial nephritis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	1 / 372 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal impairment			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
Adrenal haematoma			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Adrenal insufficiency			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperthyroidism			

subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypophysitis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
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	0 / 1 (0.00%)	0 / 7 (0.00%)	2 / 372 (0.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Myositis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Muscular weakness			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Back pain			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	2 / 372 (0.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arthralgia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	1 / 372 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteonecrosis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	1 / 372 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteonecrosis of jaw			

subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pathological fracture			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rotator cuff syndrome			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	1 / 372 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Anorectal infection			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal sepsis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	1 / 372 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Biliary sepsis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
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	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Catheter site infection			

subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	4 / 372 (1.08%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19 pneumonia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	10 / 372 (2.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 10
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 5
Campylobacter gastroenteritis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
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 viral			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	1 / 372 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium difficile colitis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Erysipelas			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	1 / 372 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Encephalitis			

subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	1 / 372 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile infection			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	1 / 372 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	1 / 372 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes zoster			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	1 / 372 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infection			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower respiratory tract infection			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	1 / 372 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myelitis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenic sepsis			

subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteomyelitis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Parainfluenzae virus infection			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	1 / 372 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peritonsillar abscess			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumocystis jirovecii pneumonia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	1 / 372 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Pneumonia			
subjects affected / exposed	0 / 1 (0.00%)	1 / 7 (14.29%)	36 / 372 (9.68%)
occurrences causally related to treatment / all	0 / 0	0 / 1	6 / 40
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 9
Pneumonia aspiration			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
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 bacterial			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	2 / 372 (0.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Pneumonia fungal			



subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
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 klebsiella			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	1 / 372 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Pulmonary sepsis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	1 / 372 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Pyelonephritis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis acute			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	1 / 372 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory tract infection			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	1 / 372 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	4 / 372 (1.08%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 2
Septic shock			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinusitis			

subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	1 / 372 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tuberculosis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Soft tissue infection			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin infection			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Varicella zoster virus infection			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urosepsis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
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	0 / 1 (0.00%)	0 / 7 (0.00%)	1 / 372 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Decreased appetite			

subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	1 / 372 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetic ketoacidosis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperkalaemia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	1 / 372 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperglycaemia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	1 / 372 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Electrolyte imbalance			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	1 / 372 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypokalaemia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemia			
subjects affected / exposed	1 / 1 (100.00%)	0 / 7 (0.00%)	3 / 372 (0.81%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Type 2 diabetes mellitus			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

<b>Non-serious adverse events</b>	Part 1 First Course: Pembrolizumab+Chemotherapy+Lenvatinib	Part 2 First Course: Pembrolizumab+Chemotherapy+Lenvatinib	Part 2 Second Course: Pembrolizumab+Chemotherapy+Lenvatinib
Total subjects affected by non-serious adverse events subjects affected / exposed	13 / 13 (100.00%)	366 / 373 (98.12%)	2 / 3 (66.67%)
<b>Vascular disorders</b>			
Orthostatic hypotension subjects affected / exposed	1 / 13 (7.69%)	1 / 373 (0.27%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Hot flush subjects affected / exposed	1 / 13 (7.69%)	2 / 373 (0.54%)	0 / 3 (0.00%)
occurrences (all)	1	2	0
Hypertension subjects affected / exposed	9 / 13 (69.23%)	110 / 373 (29.49%)	1 / 3 (33.33%)
occurrences (all)	10	158	1
<b>General disorders and administration site conditions</b>			
Asthenia subjects affected / exposed	2 / 13 (15.38%)	108 / 373 (28.95%)	0 / 3 (0.00%)
occurrences (all)	2	167	0
Chest pain subjects affected / exposed	1 / 13 (7.69%)	21 / 373 (5.63%)	0 / 3 (0.00%)
occurrences (all)	2	23	0
Gait disturbance subjects affected / exposed	1 / 13 (7.69%)	3 / 373 (0.80%)	0 / 3 (0.00%)
occurrences (all)	1	5	0
Fatigue subjects affected / exposed	8 / 13 (61.54%)	116 / 373 (31.10%)	0 / 3 (0.00%)
occurrences (all)	15	182	0
Oedema subjects affected / exposed	1 / 13 (7.69%)	7 / 373 (1.88%)	0 / 3 (0.00%)
occurrences (all)	1	7	0
Non-cardiac chest pain subjects affected / exposed	1 / 13 (7.69%)	5 / 373 (1.34%)	0 / 3 (0.00%)
occurrences (all)	1	6	0

Mucosal inflammation subjects affected / exposed occurrences (all)	2 / 13 (15.38%) 3	47 / 373 (12.60%) 62	0 / 3 (0.00%) 0
Malaise subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 2	15 / 373 (4.02%) 24	0 / 3 (0.00%) 0
Influenza like illness subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1	7 / 373 (1.88%) 11	0 / 3 (0.00%) 0
General physical health deterioration subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1	1 / 373 (0.27%) 1	0 / 3 (0.00%) 0
Extravasation subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1	0 / 373 (0.00%) 0	0 / 3 (0.00%) 0
Pyrexia subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 3	57 / 373 (15.28%) 98	0 / 3 (0.00%) 0
Pain subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1	7 / 373 (1.88%) 7	0 / 3 (0.00%) 0
Oedema peripheral subjects affected / exposed occurrences (all)	3 / 13 (23.08%) 4	61 / 373 (16.35%) 81	1 / 3 (33.33%) 1
Reproductive system and breast disorders			
Erectile dysfunction subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1	2 / 373 (0.54%) 2	0 / 3 (0.00%) 0
Pelvic pain subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1	3 / 373 (0.80%) 3	0 / 3 (0.00%) 0
Breast pain subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1	3 / 373 (0.80%) 3	0 / 3 (0.00%) 0
Respiratory, thoracic and mediastinal disorders			

Cough			
subjects affected / exposed	4 / 13 (30.77%)	65 / 373 (17.43%)	0 / 3 (0.00%)
occurrences (all)	6	82	0
Chronic obstructive pulmonary disease			
subjects affected / exposed	1 / 13 (7.69%)	3 / 373 (0.80%)	0 / 3 (0.00%)
occurrences (all)	1	3	0
Dysphonia			
subjects affected / exposed	3 / 13 (23.08%)	31 / 373 (8.31%)	0 / 3 (0.00%)
occurrences (all)	10	36	0
Dyspnoea			
subjects affected / exposed	3 / 13 (23.08%)	63 / 373 (16.89%)	0 / 3 (0.00%)
occurrences (all)	5	78	0
Dyspnoea exertional			
subjects affected / exposed	1 / 13 (7.69%)	5 / 373 (1.34%)	0 / 3 (0.00%)
occurrences (all)	1	5	0
Oropharyngeal pain			
subjects affected / exposed	3 / 13 (23.08%)	20 / 373 (5.36%)	0 / 3 (0.00%)
occurrences (all)	4	21	0
Haemoptysis			
subjects affected / exposed	1 / 13 (7.69%)	20 / 373 (5.36%)	0 / 3 (0.00%)
occurrences (all)	2	23	0
Hiccups			
subjects affected / exposed	4 / 13 (30.77%)	18 / 373 (4.83%)	0 / 3 (0.00%)
occurrences (all)	8	21	0
Immune-mediated lung disease			
subjects affected / exposed	1 / 13 (7.69%)	0 / 373 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Epistaxis			
subjects affected / exposed	3 / 13 (23.08%)	55 / 373 (14.75%)	0 / 3 (0.00%)
occurrences (all)	3	86	0
Pneumonitis			
subjects affected / exposed	0 / 13 (0.00%)	10 / 373 (2.68%)	0 / 3 (0.00%)
occurrences (all)	0	10	0
Productive cough			

subjects affected / exposed occurrences (all)	2 / 13 (15.38%) 3	15 / 373 (4.02%) 19	0 / 3 (0.00%) 0
Rhinitis allergic subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1	7 / 373 (1.88%) 7	0 / 3 (0.00%) 0
Rhinorrhoea subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1	11 / 373 (2.95%) 14	0 / 3 (0.00%) 0
Psychiatric disorders Confusional state subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1	1 / 373 (0.27%) 1	0 / 3 (0.00%) 0
Anxiety subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1	9 / 373 (2.41%) 9	0 / 3 (0.00%) 0
Insomnia subjects affected / exposed occurrences (all)	2 / 13 (15.38%) 5	26 / 373 (6.97%) 28	0 / 3 (0.00%) 0
Investigations Alanine aminotransferase increased subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	132 / 373 (35.39%) 271	0 / 3 (0.00%) 0
Amylase increased subjects affected / exposed occurrences (all)	2 / 13 (15.38%) 2	55 / 373 (14.75%) 108	0 / 3 (0.00%) 0
Aspartate aminotransferase increased subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	127 / 373 (34.05%) 311	0 / 3 (0.00%) 0
Blood alkaline phosphatase increased subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	31 / 373 (8.31%) 52	0 / 3 (0.00%) 0
Blood bilirubin increased subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	20 / 373 (5.36%) 31	0 / 3 (0.00%) 0
Blood creatinine increased			

subjects affected / exposed	5 / 13 (38.46%)	66 / 373 (17.69%)	1 / 3 (33.33%)
occurrences (all)	7	122	1
Blood glucose increased			
subjects affected / exposed	0 / 13 (0.00%)	21 / 373 (5.63%)	0 / 3 (0.00%)
occurrences (all)	0	31	0
Blood magnesium decreased			
subjects affected / exposed	0 / 13 (0.00%)	23 / 373 (6.17%)	0 / 3 (0.00%)
occurrences (all)	0	31	0
Blood thyroid stimulating hormone increased			
subjects affected / exposed	0 / 13 (0.00%)	38 / 373 (10.19%)	0 / 3 (0.00%)
occurrences (all)	0	51	0
Blood urea increased			
subjects affected / exposed	0 / 13 (0.00%)	13 / 373 (3.49%)	1 / 3 (33.33%)
occurrences (all)	0	18	1
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 13 (0.00%)	49 / 373 (13.14%)	0 / 3 (0.00%)
occurrences (all)	0	73	0
Lactescent serum			
subjects affected / exposed	1 / 13 (7.69%)	0 / 373 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Lipase increased			
subjects affected / exposed	1 / 13 (7.69%)	47 / 373 (12.60%)	0 / 3 (0.00%)
occurrences (all)	1	94	0
Lymphocyte count decreased			
subjects affected / exposed	0 / 13 (0.00%)	29 / 373 (7.77%)	0 / 3 (0.00%)
occurrences (all)	0	54	0
Neutrophil count decreased			
subjects affected / exposed	4 / 13 (30.77%)	188 / 373 (50.40%)	0 / 3 (0.00%)
occurrences (all)	6	526	0
Platelet count decreased			
subjects affected / exposed	1 / 13 (7.69%)	148 / 373 (39.68%)	0 / 3 (0.00%)
occurrences (all)	4	348	0
SARS-CoV-2 test positive			



subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1	5 / 373 (1.34%) 5	0 / 3 (0.00%) 0
Urinary occult blood positive subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	4 / 373 (1.07%) 6	0 / 3 (0.00%) 0
Weight increased subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	20 / 373 (5.36%) 30	0 / 3 (0.00%) 0
White blood cell count decreased subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	119 / 373 (31.90%) 372	0 / 3 (0.00%) 0
Weight decreased subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 2	69 / 373 (18.50%) 82	0 / 3 (0.00%) 0
Injury, poisoning and procedural complications			
Fall subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1	5 / 373 (1.34%) 5	0 / 3 (0.00%) 0
Contusion subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1	2 / 373 (0.54%) 2	0 / 3 (0.00%) 0
Head injury subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	0 / 373 (0.00%) 0	1 / 3 (33.33%) 1
Ligament injury subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1	0 / 373 (0.00%) 0	0 / 3 (0.00%) 0
Cardiac disorders			
Atrial fibrillation subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1	4 / 373 (1.07%) 9	0 / 3 (0.00%) 0
Degenerative aortic valve disease subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	1 / 373 (0.27%) 1	0 / 3 (0.00%) 0
Nervous system disorders			

Cognitive disorder			
subjects affected / exposed	1 / 13 (7.69%)	0 / 373 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Headache			
subjects affected / exposed	2 / 13 (15.38%)	45 / 373 (12.06%)	0 / 3 (0.00%)
occurrences (all)	2	64	0
Dizziness postural			
subjects affected / exposed	1 / 13 (7.69%)	1 / 373 (0.27%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Dysgeusia			
subjects affected / exposed	4 / 13 (30.77%)	26 / 373 (6.97%)	0 / 3 (0.00%)
occurrences (all)	4	28	0
Encephalitis autoimmune			
subjects affected / exposed	1 / 13 (7.69%)	0 / 373 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Dizziness			
subjects affected / exposed	3 / 13 (23.08%)	39 / 373 (10.46%)	0 / 3 (0.00%)
occurrences (all)	4	50	0
Lethargy			
subjects affected / exposed	3 / 13 (23.08%)	4 / 373 (1.07%)	0 / 3 (0.00%)
occurrences (all)	5	4	0
Neuropathy peripheral			
subjects affected / exposed	0 / 13 (0.00%)	20 / 373 (5.36%)	0 / 3 (0.00%)
occurrences (all)	0	23	0
Peripheral sensory neuropathy			
subjects affected / exposed	1 / 13 (7.69%)	6 / 373 (1.61%)	0 / 3 (0.00%)
occurrences (all)	1	7	0
Tremor			
subjects affected / exposed	1 / 13 (7.69%)	2 / 373 (0.54%)	0 / 3 (0.00%)
occurrences (all)	1	2	0
Vocal cord paralysis			
subjects affected / exposed	1 / 13 (7.69%)	0 / 373 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Post herpetic neuralgia			
subjects affected / exposed	1 / 13 (7.69%)	0 / 373 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0

Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 13 (7.69%)	192 / 373 (51.47%)	1 / 3 (33.33%)
occurrences (all)	1	394	1
Eye disorders			
Cataract			
subjects affected / exposed	1 / 13 (7.69%)	9 / 373 (2.41%)	0 / 3 (0.00%)
occurrences (all)	2	10	0
Dry eye			
subjects affected / exposed	1 / 13 (7.69%)	9 / 373 (2.41%)	0 / 3 (0.00%)
occurrences (all)	1	9	0
Eye pain			
subjects affected / exposed	1 / 13 (7.69%)	2 / 373 (0.54%)	0 / 3 (0.00%)
occurrences (all)	1	2	0
Eye pruritus			
subjects affected / exposed	1 / 13 (7.69%)	4 / 373 (1.07%)	0 / 3 (0.00%)
occurrences (all)	1	4	0
Glaucoma			
subjects affected / exposed	0 / 13 (0.00%)	0 / 373 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Lacrimation increased			
subjects affected / exposed	2 / 13 (15.38%)	24 / 373 (6.43%)	0 / 3 (0.00%)
occurrences (all)	3	25	0
Vision blurred			
subjects affected / exposed	1 / 13 (7.69%)	5 / 373 (1.34%)	0 / 3 (0.00%)
occurrences (all)	1	5	0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	2 / 13 (15.38%)	33 / 373 (8.85%)	0 / 3 (0.00%)
occurrences (all)	2	47	0
Anal incontinence			
subjects affected / exposed	1 / 13 (7.69%)	0 / 373 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Abdominal pain upper			
subjects affected / exposed	1 / 13 (7.69%)	30 / 373 (8.04%)	0 / 3 (0.00%)
occurrences (all)	2	33	0
Constipation			

subjects affected / exposed	7 / 13 (53.85%)	120 / 373 (32.17%)	1 / 3 (33.33%)
occurrences (all)	9	169	2
Dyspepsia			
subjects affected / exposed	3 / 13 (23.08%)	23 / 373 (6.17%)	0 / 3 (0.00%)
occurrences (all)	3	25	0
Dry mouth			
subjects affected / exposed	3 / 13 (23.08%)	10 / 373 (2.68%)	0 / 3 (0.00%)
occurrences (all)	3	10	0
Diarrhoea			
subjects affected / exposed	7 / 13 (53.85%)	127 / 373 (34.05%)	0 / 3 (0.00%)
occurrences (all)	10	245	0
Lip dry			
subjects affected / exposed	1 / 13 (7.69%)	0 / 373 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Glossodynia			
subjects affected / exposed	1 / 13 (7.69%)	2 / 373 (0.54%)	0 / 3 (0.00%)
occurrences (all)	3	2	0
Gingival pain			
subjects affected / exposed	1 / 13 (7.69%)	11 / 373 (2.95%)	0 / 3 (0.00%)
occurrences (all)	1	15	0
Gingival bleeding			
subjects affected / exposed	1 / 13 (7.69%)	7 / 373 (1.88%)	0 / 3 (0.00%)
occurrences (all)	2	9	0
Gastrointestinal pain			
subjects affected / exposed	1 / 13 (7.69%)	1 / 373 (0.27%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Flatulence			
subjects affected / exposed	1 / 13 (7.69%)	3 / 373 (0.80%)	0 / 3 (0.00%)
occurrences (all)	1	3	0
Dysphagia			
subjects affected / exposed	1 / 13 (7.69%)	13 / 373 (3.49%)	0 / 3 (0.00%)
occurrences (all)	1	14	0
Toothache			
subjects affected / exposed	1 / 13 (7.69%)	13 / 373 (3.49%)	0 / 3 (0.00%)
occurrences (all)	1	17	0
Vomiting			

subjects affected / exposed	5 / 13 (38.46%)	69 / 373 (18.50%)	0 / 3 (0.00%)
occurrences (all)	7	133	0
Stomatitis			
subjects affected / exposed	2 / 13 (15.38%)	47 / 373 (12.60%)	0 / 3 (0.00%)
occurrences (all)	3	64	0
Rectal ulcer			
subjects affected / exposed	1 / 13 (7.69%)	0 / 373 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Oral pain			
subjects affected / exposed	1 / 13 (7.69%)	15 / 373 (4.02%)	0 / 3 (0.00%)
occurrences (all)	1	16	0
Nausea			
subjects affected / exposed	10 / 13 (76.92%)	148 / 373 (39.68%)	0 / 3 (0.00%)
occurrences (all)	17	264	0
Skin and subcutaneous tissue disorders			
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	2 / 13 (15.38%)	13 / 373 (3.49%)	0 / 3 (0.00%)
occurrences (all)	2	13	0
Decubitus ulcer			
subjects affected / exposed	1 / 13 (7.69%)	1 / 373 (0.27%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Dry skin			
subjects affected / exposed	4 / 13 (30.77%)	14 / 373 (3.75%)	0 / 3 (0.00%)
occurrences (all)	4	14	0
Pain of skin			
subjects affected / exposed	1 / 13 (7.69%)	2 / 373 (0.54%)	0 / 3 (0.00%)
occurrences (all)	1	2	0
Alopecia			
subjects affected / exposed	2 / 13 (15.38%)	16 / 373 (4.29%)	0 / 3 (0.00%)
occurrences (all)	2	19	0
Pruritus			
subjects affected / exposed	3 / 13 (23.08%)	45 / 373 (12.06%)	0 / 3 (0.00%)
occurrences (all)	6	56	0
Rash			

subjects affected / exposed occurrences (all)	4 / 13 (30.77%) 7	64 / 373 (17.16%) 86	0 / 3 (0.00%) 0
Rash vesicular subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1	0 / 373 (0.00%) 0	0 / 3 (0.00%) 0
Skin lesion subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1	4 / 373 (1.07%) 4	0 / 3 (0.00%) 0
Renal and urinary disorders			
Dysuria subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1	10 / 373 (2.68%) 11	0 / 3 (0.00%) 0
Proteinuria subjects affected / exposed occurrences (all)	3 / 13 (23.08%) 8	55 / 373 (14.75%) 114	0 / 3 (0.00%) 0
Urinary incontinence subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1	2 / 373 (0.54%) 2	0 / 3 (0.00%) 0
Endocrine disorders			
Thyroid mass subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1	0 / 373 (0.00%) 0	0 / 3 (0.00%) 0
Hypothyroidism subjects affected / exposed occurrences (all)	5 / 13 (38.46%) 6	84 / 373 (22.52%) 104	0 / 3 (0.00%) 0
Hyperthyroidism subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1	26 / 373 (6.97%) 30	0 / 3 (0.00%) 0
Adrenal insufficiency subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1	10 / 373 (2.68%) 10	0 / 3 (0.00%) 0
Musculoskeletal and connective tissue disorders			
Arthralgia subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 2	54 / 373 (14.48%) 72	0 / 3 (0.00%) 0
Arthritis			

subjects affected / exposed	1 / 13 (7.69%)	1 / 373 (0.27%)	0 / 3 (0.00%)
occurrences (all)	2	2	0
Back pain			
subjects affected / exposed	6 / 13 (46.15%)	44 / 373 (11.80%)	0 / 3 (0.00%)
occurrences (all)	8	52	0
Myalgia			
subjects affected / exposed	0 / 13 (0.00%)	20 / 373 (5.36%)	0 / 3 (0.00%)
occurrences (all)	0	21	0
Muscle spasms			
subjects affected / exposed	1 / 13 (7.69%)	3 / 373 (0.80%)	0 / 3 (0.00%)
occurrences (all)	1	4	0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 13 (0.00%)	19 / 373 (5.09%)	0 / 3 (0.00%)
occurrences (all)	0	20	0
Joint swelling			
subjects affected / exposed	1 / 13 (7.69%)	4 / 373 (1.07%)	0 / 3 (0.00%)
occurrences (all)	1	4	0
Myositis			
subjects affected / exposed	1 / 13 (7.69%)	1 / 373 (0.27%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Neck pain			
subjects affected / exposed	0 / 13 (0.00%)	10 / 373 (2.68%)	1 / 3 (33.33%)
occurrences (all)	0	11	1
Pain in extremity			
subjects affected / exposed	2 / 13 (15.38%)	32 / 373 (8.58%)	0 / 3 (0.00%)
occurrences (all)	2	43	0
Infections and infestations			
Eye infection			
subjects affected / exposed	2 / 13 (15.38%)	2 / 373 (0.54%)	0 / 3 (0.00%)
occurrences (all)	2	2	0
Device related infection			
subjects affected / exposed	1 / 13 (7.69%)	1 / 373 (0.27%)	0 / 3 (0.00%)
occurrences (all)	1	2	0
Conjunctivitis			
subjects affected / exposed	0 / 13 (0.00%)	24 / 373 (6.43%)	0 / 3 (0.00%)
occurrences (all)	0	27	0

COVID-19			
subjects affected / exposed	1 / 13 (7.69%)	32 / 373 (8.58%)	0 / 3 (0.00%)
occurrences (all)	2	32	0
Fungal skin infection			
subjects affected / exposed	1 / 13 (7.69%)	0 / 373 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Herpes zoster			
subjects affected / exposed	1 / 13 (7.69%)	6 / 373 (1.61%)	0 / 3 (0.00%)
occurrences (all)	1	6	0
Gastroenteritis viral			
subjects affected / exposed	1 / 13 (7.69%)	0 / 373 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Gastroenteritis			
subjects affected / exposed	1 / 13 (7.69%)	4 / 373 (1.07%)	0 / 3 (0.00%)
occurrences (all)	1	4	0
Nasopharyngitis			
subjects affected / exposed	2 / 13 (15.38%)	10 / 373 (2.68%)	0 / 3 (0.00%)
occurrences (all)	3	13	0
Pneumonia			
subjects affected / exposed	1 / 13 (7.69%)	23 / 373 (6.17%)	0 / 3 (0.00%)
occurrences (all)	1	27	0
Otitis externa			
subjects affected / exposed	1 / 13 (7.69%)	0 / 373 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Oral infection			
subjects affected / exposed	1 / 13 (7.69%)	0 / 373 (0.00%)	0 / 3 (0.00%)
occurrences (all)	4	0	0
Oral herpes			
subjects affected / exposed	1 / 13 (7.69%)	1 / 373 (0.27%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Oral candidiasis			
subjects affected / exposed	1 / 13 (7.69%)	6 / 373 (1.61%)	0 / 3 (0.00%)
occurrences (all)	1	8	0
Pneumonia bacterial			
subjects affected / exposed	1 / 13 (7.69%)	0 / 373 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0



Sepsis			
subjects affected / exposed	0 / 13 (0.00%)	1 / 373 (0.27%)	1 / 3 (33.33%)
occurrences (all)	0	1	1
Viral pharyngitis			
subjects affected / exposed	1 / 13 (7.69%)	1 / 373 (0.27%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Urinary tract infection			
subjects affected / exposed	5 / 13 (38.46%)	30 / 373 (8.04%)	0 / 3 (0.00%)
occurrences (all)	11	41	0
Upper respiratory tract infection			
subjects affected / exposed	2 / 13 (15.38%)	22 / 373 (5.90%)	0 / 3 (0.00%)
occurrences (all)	2	31	0
Tooth infection			
subjects affected / exposed	1 / 13 (7.69%)	7 / 373 (1.88%)	0 / 3 (0.00%)
occurrences (all)	1	9	0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	2 / 13 (15.38%)	11 / 373 (2.95%)	1 / 3 (33.33%)
occurrences (all)	6	14	1
Decreased appetite			
subjects affected / exposed	3 / 13 (23.08%)	130 / 373 (34.85%)	0 / 3 (0.00%)
occurrences (all)	4	218	0
Hyperglycaemia			
subjects affected / exposed	0 / 13 (0.00%)	39 / 373 (10.46%)	0 / 3 (0.00%)
occurrences (all)	0	69	0
Hyperkalaemia			
subjects affected / exposed	0 / 13 (0.00%)	20 / 373 (5.36%)	0 / 3 (0.00%)
occurrences (all)	0	28	0
Hypoalbuminaemia			
subjects affected / exposed	1 / 13 (7.69%)	39 / 373 (10.46%)	0 / 3 (0.00%)
occurrences (all)	1	81	0
Hypocalcaemia			
subjects affected / exposed	1 / 13 (7.69%)	19 / 373 (5.09%)	0 / 3 (0.00%)
occurrences (all)	1	26	0
Hypomagnesaemia			

subjects affected / exposed	1 / 13 (7.69%)	36 / 373 (9.65%)	0 / 3 (0.00%)
occurrences (all)	2	59	0
Hyponatraemia			
subjects affected / exposed	2 / 13 (15.38%)	44 / 373 (11.80%)	0 / 3 (0.00%)
occurrences (all)	3	72	0
Hypoproteinaemia			
subjects affected / exposed	0 / 13 (0.00%)	11 / 373 (2.95%)	0 / 3 (0.00%)
occurrences (all)	0	11	0
Hypokalaemia			
subjects affected / exposed	1 / 13 (7.69%)	39 / 373 (10.46%)	0 / 3 (0.00%)
occurrences (all)	1	59	0

<b>Non-serious adverse events</b>	Part1 Second Course:Pembrolizumab OnlyChemotherapy+Lenvatinib	Part 2 Second Course: Pembrolizumab+Chemotherapy+Placebo	Part 2 First Course: Pembrolizumab+Chemotherapy+Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 1 (100.00%)	4 / 7 (57.14%)	363 / 372 (97.58%)
Vascular disorders			
Orthostatic hypotension			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	1 / 372 (0.27%)
occurrences (all)	0	0	1
Hot flush			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	3 / 372 (0.81%)
occurrences (all)	0	0	3
Hypertension			
subjects affected / exposed	0 / 1 (0.00%)	1 / 7 (14.29%)	44 / 372 (11.83%)
occurrences (all)	0	1	46
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	110 / 372 (29.57%)
occurrences (all)	0	0	175
Chest pain			
subjects affected / exposed	0 / 1 (0.00%)	1 / 7 (14.29%)	25 / 372 (6.72%)
occurrences (all)	0	1	29
Gait disturbance			

subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	4 / 372 (1.08%)
occurrences (all)	0	0	4
Fatigue			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	86 / 372 (23.12%)
occurrences (all)	0	0	114
Oedema			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	9 / 372 (2.42%)
occurrences (all)	0	0	11
Non-cardiac chest pain			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	9 / 372 (2.42%)
occurrences (all)	0	0	13
Mucosal inflammation			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	28 / 372 (7.53%)
occurrences (all)	0	0	35
Malaise			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	15 / 372 (4.03%)
occurrences (all)	0	0	18
Influenza like illness			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	6 / 372 (1.61%)
occurrences (all)	0	0	6
General physical health deterioration			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	1 / 372 (0.27%)
occurrences (all)	0	0	1
Extravasation			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed	0 / 1 (0.00%)	1 / 7 (14.29%)	61 / 372 (16.40%)
occurrences (all)	0	1	83
Pain			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	6 / 372 (1.61%)
occurrences (all)	0	0	6
Oedema peripheral			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	49 / 372 (13.17%)
occurrences (all)	0	0	70
Reproductive system and breast			

disorders			
Erectile dysfunction			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	1 / 372 (0.27%)
occurrences (all)	0	0	1
Pelvic pain			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	2 / 372 (0.54%)
occurrences (all)	0	0	2
Breast pain			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 1 (0.00%)	1 / 7 (14.29%)	50 / 372 (13.44%)
occurrences (all)	0	1	60
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	2 / 372 (0.54%)
occurrences (all)	0	0	4
Dysphonia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	12 / 372 (3.23%)
occurrences (all)	0	0	12
Dyspnoea			
subjects affected / exposed	0 / 1 (0.00%)	1 / 7 (14.29%)	66 / 372 (17.74%)
occurrences (all)	0	1	68
Dyspnoea exertional			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	4 / 372 (1.08%)
occurrences (all)	0	0	7
Oropharyngeal pain			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	5 / 372 (1.34%)
occurrences (all)	0	0	5
Haemoptysis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	14 / 372 (3.76%)
occurrences (all)	0	0	20
Hiccups			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	21 / 372 (5.65%)
occurrences (all)	0	0	30
Immune-mediated lung disease			

subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences (all)	0	0	0
Epistaxis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	17 / 372 (4.57%)
occurrences (all)	0	0	21
Pneumonitis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	22 / 372 (5.91%)
occurrences (all)	0	0	22
Productive cough			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	23 / 372 (6.18%)
occurrences (all)	0	0	25
Rhinitis allergic			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	1 / 372 (0.27%)
occurrences (all)	0	0	1
Rhinorrhoea			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	11 / 372 (2.96%)
occurrences (all)	0	0	12
Psychiatric disorders			
Confusional state			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	2 / 372 (0.54%)
occurrences (all)	0	0	2
Anxiety			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	9 / 372 (2.42%)
occurrences (all)	0	0	12
Insomnia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	32 / 372 (8.60%)
occurrences (all)	0	0	43
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	119 / 372 (31.99%)
occurrences (all)	0	0	251
Amylase increased			
subjects affected / exposed	0 / 1 (0.00%)	1 / 7 (14.29%)	55 / 372 (14.78%)
occurrences (all)	0	1	95
Aspartate aminotransferase increased			

subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	108 / 372 (29.03%)
occurrences (all)	0	0	240
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	31 / 372 (8.33%)
occurrences (all)	0	0	44
Blood bilirubin increased			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	9 / 372 (2.42%)
occurrences (all)	0	0	18
Blood creatinine increased			
subjects affected / exposed	0 / 1 (0.00%)	1 / 7 (14.29%)	69 / 372 (18.55%)
occurrences (all)	0	1	104
Blood glucose increased			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	22 / 372 (5.91%)
occurrences (all)	0	0	28
Blood magnesium decreased			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	17 / 372 (4.57%)
occurrences (all)	0	0	29
Blood thyroid stimulating hormone increased			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	9 / 372 (2.42%)
occurrences (all)	0	0	12
Blood urea increased			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	12 / 372 (3.23%)
occurrences (all)	0	0	21
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	30 / 372 (8.06%)
occurrences (all)	0	0	39
Lactescent serum			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences (all)	0	0	0
Lipase increased			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	43 / 372 (11.56%)
occurrences (all)	0	0	82
Lymphocyte count decreased			

subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	18 / 372 (4.84%)
occurrences (all)	0	0	31
Neutrophil count decreased			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	154 / 372 (41.40%)
occurrences (all)	0	0	436
Platelet count decreased			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	98 / 372 (26.34%)
occurrences (all)	0	0	203
SARS-CoV-2 test positive			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	4 / 372 (1.08%)
occurrences (all)	0	0	4
Urinary occult blood positive			
subjects affected / exposed	0 / 1 (0.00%)	1 / 7 (14.29%)	3 / 372 (0.81%)
occurrences (all)	0	1	4
Weight increased			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	7 / 372 (1.88%)
occurrences (all)	0	0	8
White blood cell count decreased			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	95 / 372 (25.54%)
occurrences (all)	0	0	306
Weight decreased			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	29 / 372 (7.80%)
occurrences (all)	0	0	31
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	6 / 372 (1.61%)
occurrences (all)	0	0	6
Contusion			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences (all)	0	0	0
Head injury			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	1 / 372 (0.27%)
occurrences (all)	0	0	1
Ligament injury			

subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0	0 / 7 (0.00%) 0	0 / 372 (0.00%) 0
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	1 / 372 (0.27%)
occurrences (all)	0	0	1
Degenerative aortic valve disease			
subjects affected / exposed	0 / 1 (0.00%)	1 / 7 (14.29%)	0 / 372 (0.00%)
occurrences (all)	0	1	0
Nervous system disorders			
Cognitive disorder			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	1 / 372 (0.27%)
occurrences (all)	0	0	1
Headache			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	35 / 372 (9.41%)
occurrences (all)	0	0	44
Dizziness postural			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences (all)	0	0	0
Dysgeusia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	19 / 372 (5.11%)
occurrences (all)	0	0	22
Encephalitis autoimmune			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences (all)	0	0	0
Dizziness			
subjects affected / exposed	1 / 1 (100.00%)	0 / 7 (0.00%)	36 / 372 (9.68%)
occurrences (all)	1	0	42
Lethargy			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	3 / 372 (0.81%)
occurrences (all)	0	0	3
Neuropathy peripheral			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	18 / 372 (4.84%)
occurrences (all)	0	0	19
Peripheral sensory neuropathy			



subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0	0 / 7 (0.00%) 0	8 / 372 (2.15%) 10
Tremor subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0	0 / 7 (0.00%) 0	4 / 372 (1.08%) 4
Vocal cord paralysis subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0	0 / 7 (0.00%) 0	0 / 372 (0.00%) 0
Post herpetic neuralgia subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0	0 / 7 (0.00%) 0	0 / 372 (0.00%) 0
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0	0 / 7 (0.00%) 0	220 / 372 (59.14%) 419
Eye disorders Cataract subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0	0 / 7 (0.00%) 0	7 / 372 (1.88%) 7
Dry eye subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0	1 / 7 (14.29%) 1	14 / 372 (3.76%) 14
Eye pain subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0	0 / 7 (0.00%) 0	1 / 372 (0.27%) 1
Eye pruritus subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0	0 / 7 (0.00%) 0	3 / 372 (0.81%) 3
Glaucoma subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0	1 / 7 (14.29%) 1	0 / 372 (0.00%) 0
Lacrimation increased subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0	0 / 7 (0.00%) 0	24 / 372 (6.45%) 28
Vision blurred			

subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0	0 / 7 (0.00%) 0	5 / 372 (1.34%) 6
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	20 / 372 (5.38%)
occurrences (all)	0	0	27
Anal incontinence			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences (all)	0	0	0
Abdominal pain upper			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	18 / 372 (4.84%)
occurrences (all)	0	0	20
Constipation			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	110 / 372 (29.57%)
occurrences (all)	0	0	143
Dyspepsia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	11 / 372 (2.96%)
occurrences (all)	0	0	11
Dry mouth			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	10 / 372 (2.69%)
occurrences (all)	0	0	12
Diarrhoea			
subjects affected / exposed	1 / 1 (100.00%)	0 / 7 (0.00%)	69 / 372 (18.55%)
occurrences (all)	2	0	107
Lip dry			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences (all)	0	0	0
Glossodynia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences (all)	0	0	0
Gingival pain			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	3 / 372 (0.81%)
occurrences (all)	0	0	6
Gingival bleeding			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	2 / 372 (0.54%)
occurrences (all)	0	0	2

Gastrointestinal pain subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0	0 / 7 (0.00%) 0	0 / 372 (0.00%) 0
Flatulence subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0	0 / 7 (0.00%) 0	4 / 372 (1.08%) 5
Dysphagia subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0	1 / 7 (14.29%) 1	7 / 372 (1.88%) 7
Toothache subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0	0 / 7 (0.00%) 0	7 / 372 (1.88%) 10
Vomiting subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0	0 / 7 (0.00%) 0	62 / 372 (16.67%) 99
Stomatitis subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0	0 / 7 (0.00%) 0	21 / 372 (5.65%) 30
Rectal ulcer subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0	0 / 7 (0.00%) 0	0 / 372 (0.00%) 0
Oral pain subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0	0 / 7 (0.00%) 0	2 / 372 (0.54%) 4
Nausea subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0	0 / 7 (0.00%) 0	137 / 372 (36.83%) 246
Skin and subcutaneous tissue disorders			
Palmar-plantar erythrodysaesthesia syndrome subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0	0 / 7 (0.00%) 0	3 / 372 (0.81%) 3
Decubitus ulcer subjects affected / exposed occurrences (all)	0 / 1 (0.00%) 0	0 / 7 (0.00%) 0	0 / 372 (0.00%) 0
Dry skin			

subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	13 / 372 (3.49%)
occurrences (all)	0	0	14
Pain of skin			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	1 / 372 (0.27%)
occurrences (all)	0	0	1
Alopecia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	15 / 372 (4.03%)
occurrences (all)	0	0	15
Pruritus			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	48 / 372 (12.90%)
occurrences (all)	0	0	68
Rash			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	57 / 372 (15.32%)
occurrences (all)	0	0	64
Rash vesicular			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences (all)	0	0	0
Skin lesion			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	4 / 372 (1.08%)
occurrences (all)	0	0	4
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	9 / 372 (2.42%)
occurrences (all)	0	0	10
Proteinuria			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	26 / 372 (6.99%)
occurrences (all)	0	0	37
Urinary incontinence			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	2 / 372 (0.54%)
occurrences (all)	0	0	2
Endocrine disorders			
Thyroid mass			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences (all)	0	0	0
Hypothyroidism			

subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	42 / 372 (11.29%)
occurrences (all)	0	0	46
Hyperthyroidism			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	23 / 372 (6.18%)
occurrences (all)	0	0	27
Adrenal insufficiency			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	3 / 372 (0.81%)
occurrences (all)	0	0	3
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	33 / 372 (8.87%)
occurrences (all)	0	0	38
Arthritis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	6 / 372 (1.61%)
occurrences (all)	0	0	6
Back pain			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	42 / 372 (11.29%)
occurrences (all)	0	0	47
Myalgia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	16 / 372 (4.30%)
occurrences (all)	0	0	19
Muscle spasms			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	6 / 372 (1.61%)
occurrences (all)	0	0	7
Musculoskeletal chest pain			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	7 / 372 (1.88%)
occurrences (all)	0	0	7
Joint swelling			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	1 / 372 (0.27%)
occurrences (all)	0	0	1
Myositis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences (all)	0	0	0
Neck pain			

subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	8 / 372 (2.15%)
occurrences (all)	0	0	9
Pain in extremity			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	17 / 372 (4.57%)
occurrences (all)	0	0	18
Infections and infestations			
Eye infection			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences (all)	0	0	0
Device related infection			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences (all)	0	0	0
Conjunctivitis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	18 / 372 (4.84%)
occurrences (all)	0	0	21
COVID-19			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	23 / 372 (6.18%)
occurrences (all)	0	0	24
Fungal skin infection			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences (all)	0	0	0
Herpes zoster			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	7 / 372 (1.88%)
occurrences (all)	0	0	7
Gastroenteritis viral			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	5 / 372 (1.34%)
occurrences (all)	0	0	5
Pneumonia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	21 / 372 (5.65%)
occurrences (all)	0	0	22

Otitis externa			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences (all)	0	0	0
Oral infection			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences (all)	0	0	0
Oral herpes			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	1 / 372 (0.27%)
occurrences (all)	0	0	1
Oral candidiasis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	4 / 372 (1.08%)
occurrences (all)	0	0	5
Pneumonia bacterial			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences (all)	0	0	0
Sepsis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences (all)	0	0	0
Viral pharyngitis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	0 / 372 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	29 / 372 (7.80%)
occurrences (all)	0	0	35
Upper respiratory tract infection			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	15 / 372 (4.03%)
occurrences (all)	0	0	21
Tooth infection			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	1 / 372 (0.27%)
occurrences (all)	0	0	1
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	5 / 372 (1.34%)
occurrences (all)	0	0	6
Decreased appetite			

subjects affected / exposed	0 / 1 (0.00%)	1 / 7 (14.29%)	112 / 372 (30.11%)
occurrences (all)	0	1	150
Hyperglycaemia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	33 / 372 (8.87%)
occurrences (all)	0	0	56
Hyperkalaemia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	19 / 372 (5.11%)
occurrences (all)	0	0	26
Hypoalbuminaemia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	28 / 372 (7.53%)
occurrences (all)	0	0	51
Hypocalcaemia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	18 / 372 (4.84%)
occurrences (all)	0	0	22
Hypomagnesaemia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	29 / 372 (7.80%)
occurrences (all)	0	0	42
Hyponatraemia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	31 / 372 (8.33%)
occurrences (all)	0	0	64
Hypoproteinaemia			
subjects affected / exposed	0 / 1 (0.00%)	1 / 7 (14.29%)	9 / 372 (2.42%)
occurrences (all)	0	1	20
Hypokalaemia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 7 (0.00%)	27 / 372 (7.26%)
occurrences (all)	0	0	41



## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
16 January 2019	The major changes for amendment 1 (AM 1) was in response to the feedback from the regulatory agency (FDA) regarding a potential hold comment related to permanent discontinuation of lenvatinib for Grade 3 thromboembolic events since CTCAE V5 classifies Grade 3 as "Urgent medical intervention indicated".
02 July 2019	The major changes for AM2 was to address health authority feedback and to align with the Sponsor's newly released lenvatinib and pembrolizumab (LEAP) program protocol template.
09 August 2019	The major changes for AM 3 were to correct significant clerical errors inadvertently introduced into study amendment 02 that altered the study protocol inclusion/exclusion criteria and contraceptive language.
03 March 2020	The major changes for AM 4 were to extend the enrollment period beyond the global study to achieve required exposure and number of events to investigate efficacy and safety in participants with Front-line (or first-line) (1L) NSCLC enrolled in China.
30 April 2021	The major changes for AM 5 was to update the assumptions and timing of the analyses in the SAP to allow sufficient duration of follow-up based on updated enrollment period and the long-term survival data from the reference study KEYNOTE-189.
03 September 2021	The major changes for AM6 were country specific clarifications added to address the sourcing of pembrolizumab in the UK and to clarify pembrolizumab dose modification and toxicity management in Canada.
06 October 2022	The major changes for AM 7 was Merck Sharp & Dohme Corp. entity name and address change to Merck Sharp & Dohme LLC, Rahway, NJ, USA.
27 October 2023	The major changes for AM 8 were the study to be discontinued based on the observation that the combination of pembrolizumab + platinum chemotherapy + lenvatinib versus pembrolizumab + platinum chemotherapy did not meet the prespecified criteria for the primary endpoint of OS at the final analysis and the second dual primary endpoint of PFS.

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported