Clinical trial results:
A Randomized, Double-Blind, Phase III Study of Carboplatin-Paclitaxel/Nab-Paclitaxel Chemotherapy with or without Pembrolizumab (MK-3475) in First Line Metastatic Squamous Non-small Cell Lung Cancer Subjects (KEYNOTE-407)

Summary

EudraCT number	2016-000229-38
Trial protocol	DE IT NL ES HU FR PL
Global end of trial date	14 September 2023

Results information

Result version number	v1 (current)
This version publication date	21 September 2024
First version publication date	21 September 2024

Trial information

Trial identification

Sponsor protocol code	3475-407

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02775435
WHO universal trial number (UTN)	-
Other trial identifiers	MSD: KEYNOTE-407

Notes:

Sponsors

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

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	14 September 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	14 September 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This is a study of carboplatin and paclitaxel or nano particle albumin-bound paclitaxel (nab-paclitaxel) with or without pembrolizumab (MK-3475, KEYTRUDA®) in adults with first line metastatic squamous non-small cell lung cancer (NSCLC).
The primary objective of this study was to evaluate if treatment with pembrolizumab prolongs: 1) Progression-free Survival (PFS) by Response Evaluation Criteria in Solid Tumors version 1.1 (RECIST 1.1) as assessed by a blinded central imaging vendor compared to placebo, and 2) Overall Survival (OS).

Protection of trial subjects:

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

Background therapy:

Background therapy consisted of appropriate supportive care measures as deemed necessary by the treating investigator. Supportive care measures included those for the management of AEs with potential immunologic etiology. Where appropriate, these included the use of oral or IV treatment with corticosteroids as well as additional anti-inflammatory agents if symptoms did not improve with administration of corticosteroids.

Evidence for comparator: -

Actual start date of recruitment	09 June 2016
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 19
Country: Number of subjects enrolled	Canada: 19
Country: Number of subjects enrolled	China: 15
Country: Number of subjects enrolled	France: 56
Country: Number of subjects enrolled	Germany: 18
Country: Number of subjects enrolled	Hungary: 41
Country: Number of subjects enrolled	Italy: 23
Country: Number of subjects enrolled	Japan: 50
Country: Number of subjects enrolled	Korea, Republic of: 37
Country: Number of subjects enrolled	Mexico: 21
Country: Number of subjects enrolled	Netherlands: 8
Country: Number of subjects enrolled	Poland: 36
Country: Number of subjects enrolled	Russian Federation: 50

Country: Number of subjects enrolled	Spain: 58
Country: Number of subjects enrolled	Thailand: 4
Country: Number of subjects enrolled	Türkiye: 69
Country: Number of subjects enrolled	United States: 35
Worldwide total number of subjects	559
EEA total number of subjects	240

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	254
From 65 to 84 years	302
85 years and over	3

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Per protocol, response/progression, or adverse events during the second and switch-over pembrolizumab course were not counted towards efficacy outcome measures or 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, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Pembrolizumab + Chemotherapy Combo

Arm description:

Participants received pembrolizumab 200 mg by intravenous (IV) infusion prior to chemotherapy on Day 1 of each 21-day cycle (Q3W) for up to 35 cycles (~ 2 years) PLUS Investigator’s choice of paclitaxel (200 mg/m^2 by IV infusion on Day 1 of each 21-day cycle for 4 cycles) or nab-paclitaxel (100 mg/m^2 by IV infusion on Days 1, 8, 15 of each 21-day cycle for 4 cycles) PLUS carboplatin Area Under Curve (AUC) 6 by IV infusion on Day 1 of each 21-day cycle for 4 cycles. Participants who received pembrolizumab 200 mg IV Day 1 of 21-day cycle for up to 2 years, but experienced disease progression, were eligible to receive a second course of pembrolizumab 200 mg IV Day 1 of 21-day cycle, at the investigator's discretion, for 17 cycles (~ 1 year additional).

Arm type	Experimental
Investigational medicinal product name	Pembrolizumab + Paclitaxel/nab-Paclitaxel and carboplatin Area Under Curve (AUC)
Investigational medicinal product code	
Other name	MK-3475 KEYTRUDA®
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Participants received pembrolizumab 200 mg by intravenous (IV) infusion prior to chemotherapy on Day 1 of each 21-day cycle (Q3W) for up to 35 cycles (~ 2 years) PLUS Investigator’s choice of paclitaxel (200 mg/m^2 by IV infusion on Day 1 of each 21-day cycle for 4 cycles) or nab-paclitaxel (100 mg/m^2 by IV infusion on Days 1, 8, 15 of each 21-day cycle for 4 cycles) PLUS carboplatin Area Under Curve (AUC) 6 by IV infusion on Day 1 of each 21-day cycle for 4 cycles. Participants who received pembrolizumab 200 mg IV Day 1 of 21-day cycle for up to 2 years, but experienced disease progression, were eligible to receive a second course of pembrolizumab 200 mg IV Day 1 of 21-day cycle, at the investigator's discretion, for 17 cycles (~ 1 year additional).

Arm title	Placebo + Chemotherapy

Arm description:

Participants received normal saline as placebo by IV infusion prior to chemotherapy on Day 1 of 21-day cycle for up to 35 cycles (~ 2 years) PLUS Investigator’s choice of paclitaxel (200 mg/m^2 by IV infusion on Day 1 of each 21-day cycle for 4 cycles) or nab-paclitaxel (100 mg/m^2 by IV infusion on Days 1, 8, 15 of each 21-day cycle for 4 cycles) PLUS carboplatin AUC 6 by IV infusion on Day 1 of each 21-day cycle for 4 cycles. Participants with documented disease progression following placebo chemotherapy combo could switch-over to receive pembrolizumab for up to 35 cycles (~ 2 years). Eligible cross over participants who stopped pembrolizumab and had stable disease but progressed after discontinuation, initiated a second course of pembrolizumab at the investigator's discretion for up to 17 cycles (~ 1 year additional).

Arm type	Placebo

Investigational medicinal product name	Normal saline + Paclitaxel/nab-Paclitaxel and carboplatin Area Under Curve (AUC)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Participants received normal saline as placebo by IV infusion prior to chemotherapy on Day 1 of 21-day cycle for up to 35 cycles (~ 2 years) PLUS Investigator's choice of paclitaxel (200 mg/m^2 by IV infusion on Day 1 of each 21-day cycle for 4 cycles) or nab-paclitaxel (100 mg/m^2 by IV infusion on Days 1, 8, 15 of each 21-day cycle for 4 cycles) PLUS carboplatin AUC 6 by IV infusion on Day 1 of each 21-day cycle for 4 cycles. Participants with documented disease progression following placebo chemotherapy combo could switch-over to receive pembrolizumab for up to 35 cycles (~ 2 years). Eligible cross over participants who stopped pembrolizumab and had stable disease but progressed after discontinuation, initiated a second course of pembrolizumab at the investigator's discretion for up to 17 cycles (~ 1 year additional).

Number of subjects in period 1	Pembrolizumab + Chemotherapy Combo	Placebo + Chemotherapy
Started	278	281
Treated	278	280
Received Second Course of Pembrolizumab	12	0
Switch-over + 2nd course of Pembro	0	1
Switched to Pembrolizumab+Chemotherapy	0	118
Completed	0	0
Not completed	278	281
Consent withdrawn by subject	4	9
Death	196	224
Adverse event	32	27
Sponsor Decision	44	19
Lost to follow-up	2	2

Baseline characteristics

Reporting groups	
Reporting group title	Pembrolizumab + Chemotherapy Combo
Reporting group description:	
Participants received pembrolizumab 200 mg by intravenous (IV) infusion prior to chemotherapy on Day 1 of each 21-day cycle (Q3W) for up to 35 cycles (~ 2 years) PLUS Investigator's choice of paclitaxel (200 mg/m^2 by IV infusion on Day 1 of each 21-day cycle for 4 cycles) or nab-paclitaxel (100 mg/m^2 by IV infusion on Days 1, 8, 15 of each 21-day cycle for 4 cycles) PLUS carboplatin Area Under Curve (AUC) 6 by IV infusion on Day 1 of each 21-day cycle for 4 cycles. Participants who received pembrolizumab 200 mg IV Day 1 of 21-day cycle for up to 2 years, but experienced disease progression, were eligible to receive a second course of pembrolizumab 200 mg IV Day 1 of 21-day cycle, at the investigator's discretion, for 17 cycles (~ 1 year additional).	
Reporting group title	Placebo + Chemotherapy
Reporting group description:	
Participants received normal saline as placebo by IV infusion prior to chemotherapy on Day 1 of 21-day cycle for up to 35 cycles (~ 2 years) PLUS Investigator's choice of paclitaxel (200 mg/m^2 by IV infusion on Day 1 of each 21-day cycle for 4 cycles) or nab-paclitaxel (100 mg/m^2 by IV infusion on Days 1, 8, 15 of each 21-day cycle for 4 cycles) PLUS carboplatin AUC 6 by IV infusion on Day 1 of each 21-day cycle for 4 cycles. Participants with documented disease progression following placebo chemotherapy combo could switch-over to receive pembrolizumab for up to 35 cycles (~ 2 years). Eligible cross over participants who stopped pembrolizumab and had stable disease but progressed after discontinuation, initiated a second course of pembrolizumab at the investigator's discretion for up to 17 cycles (~ 1 year additional).	

Reporting group values	Pembrolizumab + Chemotherapy Combo	Placebo + Chemotherapy	Total
Number of subjects	278	281	559
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	127	127	254
From 65-84 years	149	153	302
85 years and over	2	1	3
Age Continuous Units: Years			
arithmetic mean	65.0	64.8	
standard deviation	± 8.8	± 8.7	-
Sex: Female, Male Units: Participants			
Female	58	46	104
Male	220	235	455
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	2	2
Asian	56	52	108

Native Hawaiian or Other Pacific Islander	1	0	1
Black or African American	3	4	7
White	216	214	430
More than one race	0	0	0
Unknown or Not Reported	2	9	11
Programmed Cell Death-Ligand 1 (PD-L1) Tumor Expression Level: Tumor Proportion Score (TPS)			
Participants were assessed for their PD-L1 tumor expression level by immunohistochemistry assay using tumor tissue from a newly obtained biopsy. Participants with a TPS ≥1% were classified as PD-L1 positive and participants with a TPS <1% were classified as not PD-L1 positive.			
Units: Subjects			
TPS <1%	95	99	194
TPS ≥1%	176	177	353
Unknown	7	5	12
Taxane Chemotherapy			
Participants were classified according to their taxane chemotherapy regimen: paclitaxel or nab-paclitaxel.			
Units: Subjects			
+Paclitaxel	169	167	336
+Nab-paclitaxel	109	114	223
Geographic Region			
Participants were classified according to their geographic region: East Asia vs. non-East Asia.			
Units: Subjects			
East Asia	54	52	106
Non-East Asia	224	229	453

End points

End points reporting groups

Reporting group title	Pembrolizumab + Chemotherapy Combo

Reporting group description:

Participants received pembrolizumab 200 mg by intravenous (IV) infusion prior to chemotherapy on Day 1 of each 21-day cycle (Q3W) for up to 35 cycles (~ 2 years) PLUS Investigator’s choice of paclitaxel (200 mg/m^2 by IV infusion on Day 1 of each 21-day cycle for 4 cycles) or nab-paclitaxel (100 mg/m^2 by IV infusion on Days 1, 8, 15 of each 21-day cycle for 4 cycles) PLUS carboplatin Area Under Curve (AUC) 6 by IV infusion on Day 1 of each 21-day cycle for 4 cycles. Participants who received pembrolizumab 200 mg IV Day 1 of 21-day cycle for up to 2 years, but experienced disease progression, were eligible to receive a second course of pembrolizumab 200 mg IV Day 1 of 21-day cycle, at the investigator's discretion, for 17 cycles (~ 1 year additional).

Reporting group title	Placebo + Chemotherapy

Reporting group description:

Participants received normal saline as placebo by IV infusion prior to chemotherapy on Day 1 of 21-day cycle for up to 35 cycles (~ 2 years) PLUS Investigator’s choice of paclitaxel (200 mg/m^2 by IV infusion on Day 1 of each 21-day cycle for 4 cycles) or nab-paclitaxel (100 mg/m^2 by IV infusion on Days 1, 8, 15 of each 21-day cycle for 4 cycles) PLUS carboplatin AUC 6 by IV infusion on Day 1 of each 21-day cycle for 4 cycles. Participants with documented disease progression following placebo chemotherapy combo could switch-over to receive pembrolizumab for up to 35 cycles (~ 2 years). Eligible cross over participants who stopped pembrolizumab and had stable disease but progressed after discontinuation, initiated a second course of pembrolizumab at the investigator's discretion for up to 17 cycles (~ 1 year additional).

Primary: Progression-free Survival (PFS) as Assessed by Response Evaluation Criteria in Solid Tumors Version 1.1 (RECIST 1.1)

End point title	Progression-free Survival (PFS) as Assessed by Response Evaluation Criteria in Solid Tumors Version 1.1 (RECIST 1.1)

End point description:

PFS was defined as the time from randomization to the first documented progressive disease (PD) or death due to any cause, whichever occurred first. Per Response Criteria in Solid Tumors version 1.1 (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 have demonstrated an absolute increase of ≥5 mm. Note: The appearance of ≥1 new lesions was also considered PD. PFS as assessed by blinded independent central review per RECIST 1.1 is presented.

End point type	Primary

End point timeframe:

Up to approximately 19 months

End point values	Pembrolizumab + Chemotherapy Combo	Placebo + Chemotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	278	281		
Units: Months				
median (confidence interval 95%)	6.4 (6.2 to 8.3)	4.8 (4.3 to 5.7)		

Statistical analyses

Statistical analysis title	PFS Hazard Ratio
Comparison groups	Pembrolizumab + Chemotherapy Combo v Placebo + Chemotherapy
Number of subjects included in analysis	559
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [1]
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.56
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.45
upper limit	0.7

Notes:

[1] - Treatment comparison stratified by programmed cell death-ligand 1 (PD-L1) status (Tumor Proportion Score [TPS] ≥1% vs. <1%), taxane chemotherapy (paclitaxel vs. nab-paclitaxel) & geographic region (East Asia vs. non-East Asia)

Primary: Overall Survival (OS)

End point title	Overall Survival (OS)

End point description:

OS was defined as the time from randomization to death due to any cause. OS is presented.

End point type	Primary

End point timeframe:

Up to approximately 19 months

End point values	Pembrolizumab + Chemotherapy Combo	Placebo + Chemotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	278	281		
Units: Months				
median (confidence interval 95%)	15.9 (13.2 to 9999)	11.3 (9.5 to 14.8)		

Statistical analyses

Statistical analysis title	OS Hazard ratio
Comparison groups	Pembrolizumab + Chemotherapy Combo v Placebo + Chemotherapy

Number of subjects included in analysis	559
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0008 [2]
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.64
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.49
upper limit	0.85

Notes:

[2] - Treatment comparison stratified by programmed cell death-ligand 1 (PD-L1) status (Tumor Proportion Score [TPS] ≥1% vs. <1%), taxane chemotherapy (paclitaxel vs. nab-paclitaxel) & geographic region (East Asia vs. non-East Asia)

Secondary: Objective Response Rate (ORR) as Assessed by Response Evaluation Criteria in Solid Tumors Version 1.1 (RECIST 1.1)

End point title	Objective Response Rate (ORR) as Assessed by Response Evaluation Criteria in Solid Tumors Version 1.1 (RECIST 1.1)

End point description:

ORR was defined as the percentage of participants who had a Complete Response (CR: Disappearance of all target lesions) or a Partial Response (PR: At least a 30% decrease in the sum of diameters of target lesions) as assessed by RECIST 1.1. ORR as assessed by blinded independent central review per RECIST 1.1 is presented.

End point type	Secondary

End point timeframe:

Up to approximately 19 months

End point values	Pembrolizumab + Chemotherapy Combo	Placebo + Chemotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	278	281		
Units: Percentage of Participants				
number (confidence interval 95%)	57.9 (51.9 to 63.8)	38.4 (32.7 to 44.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (DOR) as Assessed by Response Evaluation Criteria in Solid Tumors Version 1.1 (RECIST 1.1)

End point title	Duration of Response (DOR) as Assessed by Response Evaluation Criteria in Solid Tumors Version 1.1 (RECIST 1.1)

End point description:

For participants who demonstrated a confirmed response (Complete Response [CR]: Disappearance of all target lesions or Partial Response [PR]: At least a 30% decrease in the sum of diameters of target lesions) per RECIST 1.1, DOR was defined as the time from first documented evidence of CR or PR until disease progression as assessed by RECIST 1.1 or death. DOR as assessed by blinded independent central review per RECIST 1.1 is presented.

End point type	Secondary

End point timeframe:

Up to approximately 19 months

End point values	Pembrolizumab + Chemotherapy Combo	Placebo + Chemotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	161	108		
Units: Months				
median (full range (min-max))	7.7 (1.1 to 14.7)	4.8 (1.3 to 15.8)		

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

An AE was defined as any untoward medical occurrence in a participant administered study treatment and which did not necessarily have to have a causal relationship with this treatment. The number of participants who experienced an AE is presented.

End point type	Secondary

End point timeframe:

Up to approximately 83 months

End point values	Pembrolizumab + Chemotherapy Combo	Placebo + Chemotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	278	280		
Units: Participants	274	275		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants Who Discontinued Study Treatment Due to an Adverse Event (AE)

End point title	Number of Participants Who Discontinued Study Treatment Due to an Adverse Event (AE)

End point description:

The number of participants who discontinued study treatment due to an AE is presented.

End point type	Secondary

End point timeframe:

Up to approximately 29 months

End point values	Pembrolizumab + Chemotherapy Combo	Placebo + Chemotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	278	280		
Units: Participants	80	37		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to approximately 83 months

Adverse event reporting additional description:

All-Cause Mortality (ACM): all randomized participants. AEs: all participants who got ≥1 dose of study drug. Per protocol disease progression of cancer was not considered an AE unless related to study drug; participants receiving switch-over, second course, and switch-over plus second course treatment were monitored for ACM and AEs separately.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	26.0

Reporting groups

Reporting group title	Placebo + Chemotherapy

Reporting group description:

Participants received normal saline as placebo by IV infusion prior to chemotherapy on Day 1 of each 21-day cycle for up to 35 cycles (~ 2 years) PLUS Investigator's choice of paclitaxel (200 mg/m^2 by IV infusion on Day 1 of each 21-day cycle for 4 cycles) or nab-paclitaxel (100 mg/m^2 by IV infusion on Days 1, 8, 15 of each 21-day cycle for 4 cycles) PLUS carboplatin AUC 6 by IV infusion on Day 1 of each 21-day cycle for 4 cycles.

Reporting group title	Pembrolizumab + Chemotherapy Combo

Reporting group description:

Participants received pembrolizumab 200 mg by intravenous (IV) infusion prior to chemotherapy on Day 1 of 21-day cycle for up to 35 cycles PLUS Investigator's choice of paclitaxel (200 mg/m^2 by IV infusion on Day 1 of each 21-day cycle for 4 cycles) or nab paclitaxel (100 mg/m^2 by IV infusion on Days 1, 8, 15 of each 21-day cycle for 4 cycles) PLUS carboplatin Area Under Curve (AUC) 6 by IV infusion on Day 1 of each 21-day cycle for 4 cycles.

Reporting group title	Pembrolizumab Combo (Second Course)

Reporting group description:

Participants who completed the first course of up to 35 administrations of pembrolizumab (~2 years) and were deemed to be benefitting clinically despite progression, received a second course of pembrolizumab at the investigator's discretion. Pembrolizumab was administered at 200 mg IV on Day 1 of each 21-day cycle for up to 17 cycles (up to ~1 year additional).

Reporting group title	Placebo Switched Over to Pembrolizumab (Second Course)

Reporting group description:

Participants who switched from saline placebo to complete the first course of up to 35 administrations of pembrolizumab (~2 years), initiated a second course of pembrolizumab at investigator's discretion. Pembrolizumab was administered 200 mg IV on Day 1 of each 21-day cycle for up to 17 cycles (up to ~1 year).

Reporting group title	Placebo Switched Over to Pembrolizumab

Reporting group description:

Participants who received saline placebo with chemotherapy and who experienced disease progression, switched over to receive pembrolizumab monotherapy at investigator's discretion. Pembrolizumab was administered at 200 mg IV on Day 1 of each 21-day cycle for 35 cycles (~ 2 years).

Serious adverse events	Placebo + Chemotherapy	Pembrolizumab + Chemotherapy Combo	Pembrolizumab Combo (Second Course)
Total subjects affected by serious adverse events			
subjects affected / exposed	114 / 280 (40.71%)	128 / 278 (46.04%)	2 / 12 (16.67%)
number of deaths (all causes)	143	225	6

number of deaths resulting from adverse events	20	32	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cancer pain			
subjects affected / exposed	0 / 280 (0.00%)	1 / 278 (0.36%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colon cancer			
subjects affected / exposed	1 / 280 (0.36%)	0 / 278 (0.00%)	0 / 12 (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
Tumour necrosis			
subjects affected / exposed	1 / 280 (0.36%)	0 / 278 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transitional cell carcinoma			
subjects affected / exposed	1 / 280 (0.36%)	0 / 278 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prostate cancer			
subjects affected / exposed	1 / 280 (0.36%)	0 / 278 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Paraneoplastic syndrome			
subjects affected / exposed	0 / 280 (0.00%)	0 / 278 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Arterial disorder			
subjects affected / exposed	1 / 280 (0.36%)	0 / 278 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arterial haemorrhage			

subjects affected / exposed	0 / 280 (0.00%)	0 / 278 (0.00%)	1 / 12 (8.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Embolism			
subjects affected / exposed	1 / 280 (0.36%)	1 / 278 (0.36%)	0 / 12 (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
Hypotension			
subjects affected / exposed	2 / 280 (0.71%)	2 / 278 (0.72%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	2 / 2	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Orthostatic hypotension			
subjects affected / exposed	1 / 280 (0.36%)	0 / 278 (0.00%)	0 / 12 (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
Circulatory collapse			
subjects affected / exposed	0 / 280 (0.00%)	1 / 278 (0.36%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Deep vein thrombosis			
subjects affected / exposed	0 / 280 (0.00%)	1 / 278 (0.36%)	0 / 12 (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
Thrombophlebitis migrans			
subjects affected / exposed	1 / 280 (0.36%)	0 / 278 (0.00%)	0 / 12 (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
Superficial vein thrombosis			
subjects affected / exposed	0 / 280 (0.00%)	1 / 278 (0.36%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Superior vena cava syndrome			

subjects affected / exposed	1 / 280 (0.36%)	0 / 278 (0.00%)	0 / 12 (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
Vasculitis			
subjects affected / exposed	0 / 280 (0.00%)	1 / 278 (0.36%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	2 / 280 (0.71%)	1 / 278 (0.36%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Asthenia			
subjects affected / exposed	5 / 280 (1.79%)	1 / 278 (0.36%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	4 / 5	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Death			
subjects affected / exposed	3 / 280 (1.07%)	6 / 278 (2.16%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 3	2 / 6	0 / 0
deaths causally related to treatment / all	0 / 3	2 / 6	0 / 0
Fatigue			
subjects affected / exposed	2 / 280 (0.71%)	2 / 278 (0.72%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	2 / 2	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General physical health deterioration			
subjects affected / exposed	0 / 280 (0.00%)	1 / 278 (0.36%)	0 / 12 (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
Malaise			
subjects affected / exposed	1 / 280 (0.36%)	0 / 278 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Multiple organ dysfunction syndrome			

subjects affected / exposed	1 / 280 (0.36%)	0 / 278 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	5 / 280 (1.79%)	5 / 278 (1.80%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 5	3 / 6	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oedema peripheral			
subjects affected / exposed	1 / 280 (0.36%)	0 / 278 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Amyloidosis			
subjects affected / exposed	1 / 280 (0.36%)	0 / 278 (0.00%)	0 / 12 (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
Drug hypersensitivity			
subjects affected / exposed	0 / 280 (0.00%)	2 / 278 (0.72%)	0 / 12 (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
Respiratory, thoracic and mediastinal disorders			
Atelectasis			
subjects affected / exposed	1 / 280 (0.36%)	0 / 278 (0.00%)	0 / 12 (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
Chronic obstructive pulmonary disease			
subjects affected / exposed	2 / 280 (0.71%)	3 / 278 (1.08%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis chronic			
subjects affected / exposed	1 / 280 (0.36%)	0 / 278 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Bronchial haemorrhage			
subjects affected / exposed	0 / 280 (0.00%)	1 / 278 (0.36%)	0 / 12 (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
Dyspnoea			
subjects affected / exposed	2 / 280 (0.71%)	0 / 278 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epistaxis			
subjects affected / exposed	1 / 280 (0.36%)	0 / 278 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemoptysis			
subjects affected / exposed	4 / 280 (1.43%)	6 / 278 (2.16%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 6	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonitis aspiration			
subjects affected / exposed	0 / 280 (0.00%)	1 / 278 (0.36%)	0 / 12 (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	2 / 280 (0.71%)	9 / 278 (3.24%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	1 / 2	7 / 9	0 / 0
deaths causally related to treatment / all	0 / 1	1 / 1	0 / 0
Pleural effusion			
subjects affected / exposed	2 / 280 (0.71%)	4 / 278 (1.44%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 5	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Obstructive airways disorder			
subjects affected / exposed	0 / 280 (0.00%)	1 / 278 (0.36%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Interstitial lung disease			

subjects affected / exposed	2 / 280 (0.71%)	2 / 278 (0.72%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	2 / 2	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemothorax			
subjects affected / exposed	1 / 280 (0.36%)	1 / 278 (0.36%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	3 / 280 (1.07%)	3 / 278 (1.08%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumothorax			
subjects affected / exposed	1 / 280 (0.36%)	3 / 278 (1.08%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary haemorrhage			
subjects affected / exposed	2 / 280 (0.71%)	3 / 278 (1.08%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	1 / 2	1 / 3	0 / 0
deaths causally related to treatment / all	1 / 1	1 / 2	0 / 0
Pulmonary oedema			
subjects affected / exposed	1 / 280 (0.36%)	1 / 278 (0.36%)	0 / 12 (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
Respiratory failure			
subjects affected / exposed	0 / 280 (0.00%)	4 / 278 (1.44%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 4	0 / 0
Psychiatric disorders			
Delirium			
subjects affected / exposed	2 / 280 (0.71%)	1 / 278 (0.36%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			

Alanine aminotransferase increased			
subjects affected / exposed	1 / 280 (0.36%)	0 / 278 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Infusion related reaction			
subjects affected / exposed	1 / 280 (0.36%)	5 / 278 (1.80%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	1 / 1	6 / 6	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femur fracture			
subjects affected / exposed	0 / 280 (0.00%)	0 / 278 (0.00%)	0 / 12 (0.00%)
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 compression fracture			
subjects affected / exposed	0 / 280 (0.00%)	1 / 278 (0.36%)	0 / 12 (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 myocardial infarction			
subjects affected / exposed	0 / 280 (0.00%)	0 / 278 (0.00%)	0 / 12 (0.00%)
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 coronary syndrome			
subjects affected / exposed	0 / 280 (0.00%)	1 / 278 (0.36%)	0 / 12 (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
Atrial fibrillation			
subjects affected / exposed	2 / 280 (0.71%)	0 / 278 (0.00%)	1 / 12 (8.33%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial flutter			
subjects affected / exposed	0 / 280 (0.00%)	1 / 278 (0.36%)	0 / 12 (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

Atrioventricular block			
subjects affected / exposed	0 / 280 (0.00%)	1 / 278 (0.36%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac arrest			
subjects affected / exposed	2 / 280 (0.71%)	4 / 278 (1.44%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 2	1 / 4	0 / 0
deaths causally related to treatment / all	0 / 1	1 / 4	0 / 0
Cardiac failure			
subjects affected / exposed	1 / 280 (0.36%)	2 / 278 (0.72%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 1	1 / 2	0 / 0
Cardio-respiratory arrest			
subjects affected / exposed	2 / 280 (0.71%)	0 / 278 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 2	0 / 0	0 / 0
Coronary artery disease			
subjects affected / exposed	0 / 280 (0.00%)	1 / 278 (0.36%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	0 / 280 (0.00%)	1 / 278 (0.36%)	0 / 12 (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
Prinzmetal angina			
subjects affected / exposed	1 / 280 (0.36%)	0 / 278 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pericardial effusion			
subjects affected / exposed	0 / 280 (0.00%)	1 / 278 (0.36%)	1 / 12 (8.33%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			

Balance disorder			
subjects affected / exposed	0 / 280 (0.00%)	0 / 278 (0.00%)	0 / 12 (0.00%)
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 infarction			
subjects affected / exposed	0 / 280 (0.00%)	1 / 278 (0.36%)	0 / 12 (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 ischaemia			
subjects affected / exposed	0 / 280 (0.00%)	1 / 278 (0.36%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrovascular accident			
subjects affected / exposed	0 / 280 (0.00%)	2 / 278 (0.72%)	0 / 12 (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
Dysarthria			
subjects affected / exposed	0 / 280 (0.00%)	0 / 278 (0.00%)	0 / 12 (0.00%)
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	1 / 280 (0.36%)	1 / 278 (0.36%)	0 / 12 (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
Carotid artery occlusion			
subjects affected / exposed	0 / 280 (0.00%)	1 / 278 (0.36%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Carotid artery stenosis			
subjects affected / exposed	1 / 280 (0.36%)	0 / 278 (0.00%)	0 / 12 (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
Ischaemic stroke			

subjects affected / exposed	1 / 280 (0.36%)	1 / 278 (0.36%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Intercostal neuralgia			
subjects affected / exposed	0 / 280 (0.00%)	1 / 278 (0.36%)	0 / 12 (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
Headache			
subjects affected / exposed	1 / 280 (0.36%)	0 / 278 (0.00%)	0 / 12 (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
Facial paralysis			
subjects affected / exposed	0 / 280 (0.00%)	0 / 278 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neuropathy peripheral			
subjects affected / exposed	0 / 280 (0.00%)	1 / 278 (0.36%)	0 / 12 (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
Sciatica			
subjects affected / exposed	0 / 280 (0.00%)	1 / 278 (0.36%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seizure			
subjects affected / exposed	0 / 280 (0.00%)	3 / 278 (1.08%)	0 / 12 (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
Uraemic encephalopathy			
subjects affected / exposed	1 / 280 (0.36%)	0 / 278 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient ischaemic attack			

subjects affected / exposed	1 / 280 (0.36%)	1 / 278 (0.36%)	0 / 12 (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
Syncope			
subjects affected / exposed	2 / 280 (0.71%)	1 / 278 (0.36%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal cord compression			
subjects affected / exposed	0 / 280 (0.00%)	1 / 278 (0.36%)	0 / 12 (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
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	7 / 280 (2.50%)	5 / 278 (1.80%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	5 / 7	5 / 5	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Autoimmune haemolytic anaemia			
subjects affected / exposed	0 / 280 (0.00%)	1 / 278 (0.36%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenia			
subjects affected / exposed	8 / 280 (2.86%)	7 / 278 (2.52%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	9 / 9	8 / 8	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Splenic haematoma			
subjects affected / exposed	0 / 280 (0.00%)	0 / 278 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopenia			
subjects affected / exposed	3 / 280 (1.07%)	6 / 278 (2.16%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	4 / 4	7 / 7	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile neutropenia			

subjects affected / exposed	10 / 280 (3.57%)	15 / 278 (5.40%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	11 / 12	14 / 15	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eosinophilia			
subjects affected / exposed	0 / 280 (0.00%)	1 / 278 (0.36%)	0 / 12 (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
Leukopenia			
subjects affected / exposed	0 / 280 (0.00%)	4 / 278 (1.44%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	4 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Cataract			
subjects affected / exposed	0 / 280 (0.00%)	0 / 278 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 280 (0.36%)	0 / 278 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Autoimmune colitis			
subjects affected / exposed	0 / 280 (0.00%)	1 / 278 (0.36%)	0 / 12 (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
Duodenal ulcer			
subjects affected / exposed	1 / 280 (0.36%)	0 / 278 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	6 / 280 (2.14%)	8 / 278 (2.88%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	4 / 6	6 / 9	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Constipation			

subjects affected / exposed	0 / 280 (0.00%)	0 / 278 (0.00%)	0 / 12 (0.00%)
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	1 / 280 (0.36%)	6 / 278 (2.16%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	1 / 1	6 / 6	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Duodenitis			
subjects affected / exposed	0 / 280 (0.00%)	2 / 278 (0.72%)	0 / 12 (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
Gastric ulcer haemorrhage			
subjects affected / exposed	1 / 280 (0.36%)	0 / 278 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enterocolitis			
subjects affected / exposed	1 / 280 (0.36%)	1 / 278 (0.36%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dysphagia			
subjects affected / exposed	1 / 280 (0.36%)	0 / 278 (0.00%)	0 / 12 (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
Ileus			
subjects affected / exposed	1 / 280 (0.36%)	0 / 278 (0.00%)	0 / 12 (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
Pneumatosis intestinalis			
subjects affected / exposed	1 / 280 (0.36%)	0 / 278 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophageal stenosis			

subjects affected / exposed	0 / 280 (0.00%)	1 / 278 (0.36%)	0 / 12 (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
Nausea			
subjects affected / exposed	1 / 280 (0.36%)	0 / 278 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal perforation			
subjects affected / exposed	0 / 280 (0.00%)	1 / 278 (0.36%)	0 / 12 (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
Vomiting			
subjects affected / exposed	3 / 280 (1.07%)	0 / 278 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	1 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Autoimmune hepatitis			
subjects affected / exposed	0 / 280 (0.00%)	3 / 278 (1.08%)	0 / 12 (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
Bile duct stone			
subjects affected / exposed	1 / 280 (0.36%)	0 / 278 (0.00%)	0 / 12 (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
Cholelithiasis			
subjects affected / exposed	0 / 280 (0.00%)	1 / 278 (0.36%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis acute			
subjects affected / exposed	0 / 280 (0.00%)	1 / 278 (0.36%)	0 / 12 (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 / 280 (0.00%)	0 / 278 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholangitis			
subjects affected / exposed	1 / 280 (0.36%)	0 / 278 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic failure			
subjects affected / exposed	0 / 280 (0.00%)	1 / 278 (0.36%)	0 / 12 (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
Hepatitis			
subjects affected / exposed	0 / 280 (0.00%)	0 / 278 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperbilirubinaemia			
subjects affected / exposed	0 / 280 (0.00%)	0 / 278 (0.00%)	1 / 12 (8.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Diabetic foot			
subjects affected / exposed	1 / 280 (0.36%)	0 / 278 (0.00%)	0 / 12 (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
Psoriasis			
subjects affected / exposed	0 / 280 (0.00%)	1 / 278 (0.36%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rash maculo-papular			
subjects affected / exposed	0 / 280 (0.00%)	1 / 278 (0.36%)	0 / 12 (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
Renal and urinary disorders			

Haematuria			
subjects affected / exposed	1 / 280 (0.36%)	0 / 278 (0.00%)	0 / 12 (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
Glomerulonephritis membranous			
subjects affected / exposed	1 / 280 (0.36%)	0 / 278 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute kidney injury			
subjects affected / exposed	4 / 280 (1.43%)	2 / 278 (0.72%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	3 / 4	2 / 3	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Nephritis			
subjects affected / exposed	1 / 280 (0.36%)	1 / 278 (0.36%)	0 / 12 (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
Tubulointerstitial nephritis			
subjects affected / exposed	0 / 280 (0.00%)	1 / 278 (0.36%)	0 / 12 (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 retention			
subjects affected / exposed	1 / 280 (0.36%)	0 / 278 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
Autoimmune thyroiditis			
subjects affected / exposed	0 / 280 (0.00%)	1 / 278 (0.36%)	0 / 12 (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
Hyperthyroidism			
subjects affected / exposed	0 / 280 (0.00%)	1 / 278 (0.36%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Inappropriate antidiuretic hormone			

secretion			
subjects affected / exposed	0 / 280 (0.00%)	1 / 278 (0.36%)	0 / 12 (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
Hypothyroidism			
subjects affected / exposed	0 / 280 (0.00%)	1 / 278 (0.36%)	0 / 12 (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
Hypopituitarism			
subjects affected / exposed	0 / 280 (0.00%)	1 / 278 (0.36%)	0 / 12 (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 / 280 (0.00%)	1 / 278 (0.36%)	0 / 12 (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			
Myalgia			
subjects affected / exposed	1 / 280 (0.36%)	0 / 278 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematoma muscle			
subjects affected / exposed	1 / 280 (0.36%)	0 / 278 (0.00%)	0 / 12 (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
Back pain			
subjects affected / exposed	1 / 280 (0.36%)	2 / 278 (0.72%)	0 / 12 (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
Arthralgia			
subjects affected / exposed	0 / 280 (0.00%)	2 / 278 (0.72%)	0 / 12 (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

Pathological fracture			
subjects affected / exposed	1 / 280 (0.36%)	0 / 278 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Appendiceal abscess			
subjects affected / exposed	0 / 280 (0.00%)	1 / 278 (0.36%)	0 / 12 (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
Biliary tract infection			
subjects affected / exposed	0 / 280 (0.00%)	1 / 278 (0.36%)	0 / 12 (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
Blister infected			
subjects affected / exposed	0 / 280 (0.00%)	1 / 278 (0.36%)	0 / 12 (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			
subjects affected / exposed	1 / 280 (0.36%)	0 / 278 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19 pneumonia			
subjects affected / exposed	0 / 280 (0.00%)	0 / 278 (0.00%)	1 / 12 (8.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Campylobacter colitis			
subjects affected / exposed	0 / 280 (0.00%)	1 / 278 (0.36%)	0 / 12 (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
Candida infection			
subjects affected / exposed	1 / 280 (0.36%)	0 / 278 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium difficile colitis			

subjects affected / exposed	0 / 280 (0.00%)	1 / 278 (0.36%)	0 / 12 (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
Device related infection			
subjects affected / exposed	2 / 280 (0.71%)	0 / 278 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatitis B			
subjects affected / exposed	1 / 280 (0.36%)	0 / 278 (0.00%)	0 / 12 (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
Hepatitis E			
subjects affected / exposed	0 / 280 (0.00%)	1 / 278 (0.36%)	0 / 12 (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
Necrotising fasciitis			
subjects affected / exposed	0 / 280 (0.00%)	1 / 278 (0.36%)	0 / 12 (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
Infection			
subjects affected / exposed	0 / 280 (0.00%)	0 / 278 (0.00%)	1 / 12 (8.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Kidney infection			
subjects affected / exposed	1 / 280 (0.36%)	0 / 278 (0.00%)	0 / 12 (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
Klebsiella infection			
subjects affected / exposed	1 / 280 (0.36%)	0 / 278 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestine infection			

subjects affected / exposed	0 / 280 (0.00%)	0 / 278 (0.00%)	0 / 12 (0.00%)
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	1 / 280 (0.36%)	1 / 278 (0.36%)	0 / 12 (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
Lung abscess			
subjects affected / exposed	1 / 280 (0.36%)	2 / 278 (0.72%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Meningitis pneumococcal			
subjects affected / exposed	1 / 280 (0.36%)	0 / 278 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary sepsis			
subjects affected / exposed	1 / 280 (0.36%)	2 / 278 (0.72%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Prostatic abscess			
subjects affected / exposed	1 / 280 (0.36%)	0 / 278 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia legionella			
subjects affected / exposed	0 / 280 (0.00%)	1 / 278 (0.36%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia klebsiella			
subjects affected / exposed	1 / 280 (0.36%)	0 / 278 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia fungal			

subjects affected / exposed	1 / 280 (0.36%)	0 / 278 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Pneumonia bacterial			
subjects affected / exposed	1 / 280 (0.36%)	2 / 278 (0.72%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	21 / 280 (7.50%)	22 / 278 (7.91%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	5 / 23	8 / 23	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 2	0 / 0
Pyelonephritis			
subjects affected / exposed	0 / 280 (0.00%)	1 / 278 (0.36%)	0 / 12 (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
Oral candidiasis			
subjects affected / exposed	1 / 280 (0.36%)	0 / 278 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	1 / 280 (0.36%)	2 / 278 (0.72%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	0 / 280 (0.00%)	2 / 278 (0.72%)	0 / 12 (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
Tracheobronchitis			
subjects affected / exposed	0 / 280 (0.00%)	0 / 278 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stoma site infection			

subjects affected / exposed	0 / 280 (0.00%)	0 / 278 (0.00%)	1 / 12 (8.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic shock			
subjects affected / exposed	3 / 280 (1.07%)	1 / 278 (0.36%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	2 / 3	0 / 1	0 / 0
deaths causally related to treatment / all	2 / 3	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	2 / 280 (0.71%)	6 / 278 (2.16%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 2	4 / 6	0 / 0
deaths causally related to treatment / all	0 / 1	3 / 4	0 / 0
Respiratory tract infection			
subjects affected / exposed	0 / 280 (0.00%)	1 / 278 (0.36%)	0 / 12 (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 / 280 (0.00%)	1 / 278 (0.36%)	0 / 12 (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
Vascular device infection			
subjects affected / exposed	0 / 280 (0.00%)	0 / 278 (0.00%)	0 / 12 (0.00%)
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			
Decreased appetite			
subjects affected / exposed	1 / 280 (0.36%)	1 / 278 (0.36%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dehydration			
subjects affected / exposed	1 / 280 (0.36%)	0 / 278 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetes mellitus			

subjects affected / exposed	1 / 280 (0.36%)	1 / 278 (0.36%)	0 / 12 (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
Hypokalaemia			
subjects affected / exposed	0 / 280 (0.00%)	0 / 278 (0.00%)	0 / 12 (0.00%)
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	2 / 280 (0.71%)	1 / 278 (0.36%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypercalcaemia			
subjects affected / exposed	5 / 280 (1.79%)	0 / 278 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 5	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemia			
subjects affected / exposed	3 / 280 (1.07%)	2 / 278 (0.72%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	1 / 3	3 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Placebo Switched Over to Pembrolizumab (Second Course)	Placebo Switched Over to Pembrolizumab	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 1 (0.00%)	35 / 118 (29.66%)	
number of deaths (all causes)	0	111	
number of deaths resulting from adverse events	0	7	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cancer pain			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colon cancer			

subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tumour necrosis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transitional cell carcinoma			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostate cancer			
subjects affected / exposed	0 / 1 (0.00%)	1 / 118 (0.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Paraneoplastic syndrome			
subjects affected / exposed	0 / 1 (0.00%)	1 / 118 (0.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Arterial disorder			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arterial haemorrhage			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Embolism			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypotension			

subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Orthostatic hypotension			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Circulatory collapse			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Deep vein thrombosis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombophlebitis migrans			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Superficial vein thrombosis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Superior vena cava syndrome			
subjects affected / exposed	0 / 1 (0.00%)	1 / 118 (0.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Vasculitis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Chest pain			

subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Asthenia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Death			
subjects affected / exposed	0 / 1 (0.00%)	1 / 118 (0.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Fatigue			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General physical health deterioration			
subjects affected / exposed	0 / 1 (0.00%)	1 / 118 (0.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malaise			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple organ dysfunction syndrome			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oedema peripheral			

subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Amyloidosis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Drug hypersensitivity			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Atelectasis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 1 (0.00%)	2 / 118 (1.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Bronchitis chronic			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchial haemorrhage			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Epistaxis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemoptysis			
subjects affected / exposed	0 / 1 (0.00%)	2 / 118 (1.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonitis aspiration			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonitis			
subjects affected / exposed	0 / 1 (0.00%)	5 / 118 (4.24%)	
occurrences causally related to treatment / all	0 / 0	5 / 5	
deaths causally related to treatment / all	0 / 0	2 / 2	
Pleural effusion			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Obstructive airways disorder			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Interstitial lung disease			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemothorax			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			

subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumothorax			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary haemorrhage			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary oedema			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	0 / 1 (0.00%)	1 / 118 (0.85%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Delirium			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Infusion related reaction			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Femur fracture			
subjects affected / exposed	0 / 1 (0.00%)	1 / 118 (0.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal compression fracture			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	0 / 1 (0.00%)	1 / 118 (0.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Acute coronary syndrome			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial flutter			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrioventricular block			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac arrest			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure			

subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardio-respiratory arrest			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery disease			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prinzmetal angina			
subjects affected / exposed	0 / 1 (0.00%)	1 / 118 (0.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericardial effusion			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Balance disorder			
subjects affected / exposed	0 / 1 (0.00%)	1 / 118 (0.85%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral infarction			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral ischaemia			

subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrovascular accident			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysarthria			
subjects affected / exposed	0 / 1 (0.00%)	1 / 118 (0.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epilepsy			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carotid artery occlusion			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carotid artery stenosis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic stroke			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intercostal neuralgia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Headache			

subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Facial paralysis			
subjects affected / exposed	0 / 1 (0.00%)	1 / 118 (0.85%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neuropathy peripheral			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sciatica			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seizure			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uraemic encephalopathy			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient ischaemic attack			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal cord compression			

subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 1 (0.00%)	1 / 118 (0.85%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Autoimmune haemolytic anaemia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Splenic haematoma			
subjects affected / exposed	0 / 1 (0.00%)	1 / 118 (0.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile neutropenia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eosinophilia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Leukopenia			

subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Cataract			
subjects affected / exposed	0 / 1 (0.00%)	1 / 118 (0.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Autoimmune colitis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenal ulcer			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Constipation			
subjects affected / exposed	0 / 1 (0.00%)	1 / 118 (0.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenitis			

subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric ulcer haemorrhage			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterocolitis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysphagia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileus			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumatosis intestinalis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal stenosis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal perforation			

subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Autoimmune hepatitis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bile duct stone			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholelithiasis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis acute			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis			
subjects affected / exposed	0 / 1 (0.00%)	1 / 118 (0.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholangitis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic failure			

subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis			
subjects affected / exposed	0 / 1 (0.00%)	1 / 118 (0.85%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperbilirubinaemia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Diabetic foot			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psoriasis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rash maculo-papular			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Glomerulonephritis membranous			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute kidney injury			

subjects affected / exposed	0 / 1 (0.00%)	1 / 118 (0.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephritis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tubulointerstitial nephritis			
subjects affected / exposed	0 / 1 (0.00%)	1 / 118 (0.85%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary retention			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Autoimmune thyroiditis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperthyroidism			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inappropriate antidiuretic hormone secretion			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypothyroidism			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypopituitarism			

subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypophysitis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Myalgia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematoma muscle			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Back pain			
subjects affected / exposed	0 / 1 (0.00%)	2 / 118 (1.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthralgia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pathological fracture			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Appendiceal abscess			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Biliary tract infection			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blister infected			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	0 / 1 (0.00%)	1 / 118 (0.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19 pneumonia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Campylobacter colitis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Candida infection			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium difficile colitis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device related infection			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis B			

subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis E			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Necrotising fasciitis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infection			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Kidney infection			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Klebsiella infection			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestine infection			
subjects affected / exposed	0 / 1 (0.00%)	1 / 118 (0.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung abscess			

subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningitis pneumococcal			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary sepsis			
subjects affected / exposed	0 / 1 (0.00%)	1 / 118 (0.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Prostatic abscess			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia legionella			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia klebsiella			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia fungal			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia bacterial			
subjects affected / exposed	0 / 1 (0.00%)	1 / 118 (0.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			

subjects affected / exposed	0 / 1 (0.00%)	7 / 118 (5.93%)	
occurrences causally related to treatment / all	0 / 0	0 / 9	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oral candidiasis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	0 / 1 (0.00%)	1 / 118 (0.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tracheobronchitis			
subjects affected / exposed	0 / 1 (0.00%)	1 / 118 (0.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stoma site infection			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic shock			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			

subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory tract infection			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urosepsis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular device infection			
subjects affected / exposed	0 / 1 (0.00%)	1 / 118 (0.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 1 (0.00%)	1 / 118 (0.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dehydration			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetes mellitus			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypokalaemia			
subjects affected / exposed	0 / 1 (0.00%)	1 / 118 (0.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperkalaemia			

subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypercalcaemia			
subjects affected / exposed	0 / 1 (0.00%)	1 / 118 (0.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyponatraemia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Placebo + Chemotherapy	Pembrolizumab + Chemotherapy Combo	Pembrolizumab Combo (Second Course)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	272 / 280 (97.14%)	270 / 278 (97.12%)	9 / 12 (75.00%)
Vascular disorders			
Hypotension			
subjects affected / exposed	16 / 280 (5.71%)	12 / 278 (4.32%)	1 / 12 (8.33%)
occurrences (all)	19	13	1
Hypertension			
subjects affected / exposed	14 / 280 (5.00%)	18 / 278 (6.47%)	0 / 12 (0.00%)
occurrences (all)	15	22	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	60 / 280 (21.43%)	62 / 278 (22.30%)	0 / 12 (0.00%)
occurrences (all)	72	83	0
Chest pain			
subjects affected / exposed	24 / 280 (8.57%)	20 / 278 (7.19%)	0 / 12 (0.00%)
occurrences (all)	24	21	0
Fatigue			
subjects affected / exposed	72 / 280 (25.71%)	67 / 278 (24.10%)	1 / 12 (8.33%)
occurrences (all)	102	92	2

Oedema peripheral			
subjects affected / exposed	22 / 280 (7.86%)	26 / 278 (9.35%)	0 / 12 (0.00%)
occurrences (all)	30	27	0
Pyrexia			
subjects affected / exposed	35 / 280 (12.50%)	39 / 278 (14.03%)	0 / 12 (0.00%)
occurrences (all)	41	45	0
Respiratory, thoracic and mediastinal disorders			
Haemoptysis			
subjects affected / exposed	25 / 280 (8.93%)	23 / 278 (8.27%)	1 / 12 (8.33%)
occurrences (all)	36	24	1
Epistaxis			
subjects affected / exposed	19 / 280 (6.79%)	27 / 278 (9.71%)	0 / 12 (0.00%)
occurrences (all)	21	32	0
Dyspnoea			
subjects affected / exposed	45 / 280 (16.07%)	41 / 278 (14.75%)	2 / 12 (16.67%)
occurrences (all)	49	46	2
Cough			
subjects affected / exposed	56 / 280 (20.00%)	49 / 278 (17.63%)	0 / 12 (0.00%)
occurrences (all)	66	55	0
Lung infiltration			
subjects affected / exposed	0 / 280 (0.00%)	0 / 278 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Hiccups			
subjects affected / exposed	6 / 280 (2.14%)	14 / 278 (5.04%)	0 / 12 (0.00%)
occurrences (all)	6	21	0
Productive cough			
subjects affected / exposed	13 / 280 (4.64%)	18 / 278 (6.47%)	0 / 12 (0.00%)
occurrences (all)	15	21	0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	23 / 280 (8.21%)	31 / 278 (11.15%)	0 / 12 (0.00%)
occurrences (all)	24	32	0
Anxiety			
subjects affected / exposed	8 / 280 (2.86%)	15 / 278 (5.40%)	0 / 12 (0.00%)
occurrences (all)	9	17	0
Investigations			

Alanine aminotransferase increased			
subjects affected / exposed	12 / 280 (4.29%)	23 / 278 (8.27%)	2 / 12 (16.67%)
occurrences (all)	12	39	3
White blood cell count decreased			
subjects affected / exposed	32 / 280 (11.43%)	32 / 278 (11.51%)	1 / 12 (8.33%)
occurrences (all)	61	78	4
Blood alkaline phosphatase increased			
subjects affected / exposed	12 / 280 (4.29%)	12 / 278 (4.32%)	1 / 12 (8.33%)
occurrences (all)	12	19	2
Blood bilirubin increased			
subjects affected / exposed	3 / 280 (1.07%)	5 / 278 (1.80%)	1 / 12 (8.33%)
occurrences (all)	6	13	2
Blood creatinine increased			
subjects affected / exposed	15 / 280 (5.36%)	26 / 278 (9.35%)	1 / 12 (8.33%)
occurrences (all)	24	37	4
Weight decreased			
subjects affected / exposed	24 / 280 (8.57%)	31 / 278 (11.15%)	1 / 12 (8.33%)
occurrences (all)	24	33	1
Platelet count decreased			
subjects affected / exposed	23 / 280 (8.21%)	25 / 278 (8.99%)	1 / 12 (8.33%)
occurrences (all)	42	52	2
Neutrophil count decreased			
subjects affected / exposed	28 / 280 (10.00%)	24 / 278 (8.63%)	0 / 12 (0.00%)
occurrences (all)	60	59	0
Aspartate aminotransferase increased			
subjects affected / exposed	16 / 280 (5.71%)	26 / 278 (9.35%)	2 / 12 (16.67%)
occurrences (all)	17	40	2
Nervous system disorders			
Dizziness			
subjects affected / exposed	20 / 280 (7.14%)	21 / 278 (7.55%)	0 / 12 (0.00%)
occurrences (all)	23	25	0
Peripheral sensory neuropathy			
subjects affected / exposed	37 / 280 (13.21%)	33 / 278 (11.87%)	0 / 12 (0.00%)
occurrences (all)	39	34	0
Paraesthesia			

subjects affected / exposed	16 / 280 (5.71%)	21 / 278 (7.55%)	0 / 12 (0.00%)
occurrences (all)	17	22	0
Neuropathy peripheral			
subjects affected / exposed	48 / 280 (17.14%)	60 / 278 (21.58%)	0 / 12 (0.00%)
occurrences (all)	56	69	0
Dysgeusia			
subjects affected / exposed	11 / 280 (3.93%)	24 / 278 (8.63%)	0 / 12 (0.00%)
occurrences (all)	11	27	0
Headache			
subjects affected / exposed	23 / 280 (8.21%)	25 / 278 (8.99%)	0 / 12 (0.00%)
occurrences (all)	27	28	0
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	85 / 280 (30.36%)	99 / 278 (35.61%)	0 / 12 (0.00%)
occurrences (all)	166	201	0
Leukopenia			
subjects affected / exposed	20 / 280 (7.14%)	20 / 278 (7.19%)	0 / 12 (0.00%)
occurrences (all)	40	46	0
Anaemia			
subjects affected / exposed	139 / 280 (49.64%)	148 / 278 (53.24%)	1 / 12 (8.33%)
occurrences (all)	186	200	1
Thrombocytopenia			
subjects affected / exposed	64 / 280 (22.86%)	81 / 278 (29.14%)	1 / 12 (8.33%)
occurrences (all)	95	131	1
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	17 / 280 (6.07%)	22 / 278 (7.91%)	0 / 12 (0.00%)
occurrences (all)	17	24	0
Vomiting			
subjects affected / exposed	30 / 280 (10.71%)	51 / 278 (18.35%)	0 / 12 (0.00%)
occurrences (all)	47	71	0
Stomatitis			
subjects affected / exposed	15 / 280 (5.36%)	14 / 278 (5.04%)	0 / 12 (0.00%)
occurrences (all)	16	17	0
Nausea			

subjects affected / exposed	90 / 280 (32.14%)	101 / 278 (36.33%)	0 / 12 (0.00%)
occurrences (all)	136	151	0
Dysphagia			
subjects affected / exposed	6 / 280 (2.14%)	5 / 278 (1.80%)	1 / 12 (8.33%)
occurrences (all)	7	5	1
Dry mouth			
subjects affected / exposed	3 / 280 (1.07%)	10 / 278 (3.60%)	0 / 12 (0.00%)
occurrences (all)	3	12	0
Diarrhoea			
subjects affected / exposed	65 / 280 (23.21%)	88 / 278 (31.65%)	0 / 12 (0.00%)
occurrences (all)	86	141	0
Constipation			
subjects affected / exposed	62 / 280 (22.14%)	70 / 278 (25.18%)	0 / 12 (0.00%)
occurrences (all)	74	93	0
Hepatobiliary disorders			
Cholestasis			
subjects affected / exposed	0 / 280 (0.00%)	1 / 278 (0.36%)	1 / 12 (8.33%)
occurrences (all)	0	1	1
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	32 / 280 (11.43%)	52 / 278 (18.71%)	1 / 12 (8.33%)
occurrences (all)	37	62	1
Pruritus			
subjects affected / exposed	25 / 280 (8.93%)	51 / 278 (18.35%)	0 / 12 (0.00%)
occurrences (all)	29	61	0
Dry skin			
subjects affected / exposed	8 / 280 (2.86%)	12 / 278 (4.32%)	1 / 12 (8.33%)
occurrences (all)	8	12	1
Alopecia			
subjects affected / exposed	105 / 280 (37.50%)	128 / 278 (46.04%)	0 / 12 (0.00%)
occurrences (all)	106	129	0
Skin necrosis			
subjects affected / exposed	0 / 280 (0.00%)	0 / 278 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Endocrine disorders			

Hypothyroidism			
subjects affected / exposed	6 / 280 (2.14%)	33 / 278 (11.87%)	0 / 12 (0.00%)
occurrences (all)	7	36	0
Hyperthyroidism			
subjects affected / exposed	2 / 280 (0.71%)	20 / 278 (7.19%)	0 / 12 (0.00%)
occurrences (all)	2	22	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	48 / 280 (17.14%)	70 / 278 (25.18%)	0 / 12 (0.00%)
occurrences (all)	61	103	0
Back pain			
subjects affected / exposed	37 / 280 (13.21%)	24 / 278 (8.63%)	0 / 12 (0.00%)
occurrences (all)	38	24	0
Myalgia			
subjects affected / exposed	34 / 280 (12.14%)	37 / 278 (13.31%)	0 / 12 (0.00%)
occurrences (all)	41	47	0
Pain in extremity			
subjects affected / exposed	27 / 280 (9.64%)	23 / 278 (8.27%)	0 / 12 (0.00%)
occurrences (all)	36	31	0
Polyarthritis			
subjects affected / exposed	0 / 280 (0.00%)	0 / 278 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Infections and infestations			
Bronchitis			
subjects affected / exposed	11 / 280 (3.93%)	22 / 278 (7.91%)	0 / 12 (0.00%)
occurrences (all)	12	25	0
Nasopharyngitis			
subjects affected / exposed	7 / 280 (2.50%)	20 / 278 (7.19%)	0 / 12 (0.00%)
occurrences (all)	7	27	0
Pneumonia			
subjects affected / exposed	16 / 280 (5.71%)	14 / 278 (5.04%)	0 / 12 (0.00%)
occurrences (all)	16	16	0
Stoma site infection			
subjects affected / exposed	0 / 280 (0.00%)	0 / 278 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Upper respiratory tract infection			

subjects affected / exposed	10 / 280 (3.57%)	20 / 278 (7.19%)	0 / 12 (0.00%)
occurrences (all)	13	30	0
Urinary tract infection			
subjects affected / exposed	8 / 280 (2.86%)	16 / 278 (5.76%)	1 / 12 (8.33%)
occurrences (all)	9	17	2
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	82 / 280 (29.29%)	77 / 278 (27.70%)	0 / 12 (0.00%)
occurrences (all)	101	120	0
Hypercalcaemia			
subjects affected / exposed	7 / 280 (2.50%)	8 / 278 (2.88%)	0 / 12 (0.00%)
occurrences (all)	8	9	0
Hyperglycaemia			
subjects affected / exposed	12 / 280 (4.29%)	11 / 278 (3.96%)	1 / 12 (8.33%)
occurrences (all)	13	14	1
Hypoalbuminaemia			
subjects affected / exposed	12 / 280 (4.29%)	15 / 278 (5.40%)	0 / 12 (0.00%)
occurrences (all)	19	21	0
Hypocalcaemia			
subjects affected / exposed	18 / 280 (6.43%)	7 / 278 (2.52%)	0 / 12 (0.00%)
occurrences (all)	27	13	0
Hypokalaemia			
subjects affected / exposed	19 / 280 (6.79%)	18 / 278 (6.47%)	0 / 12 (0.00%)
occurrences (all)	28	31	0
Hypomagnesaemia			
subjects affected / exposed	21 / 280 (7.50%)	24 / 278 (8.63%)	1 / 12 (8.33%)
occurrences (all)	27	36	1
Hyponatraemia			
subjects affected / exposed	13 / 280 (4.64%)	20 / 278 (7.19%)	2 / 12 (16.67%)
occurrences (all)	14	28	2
Hypophosphataemia			
subjects affected / exposed	11 / 280 (3.93%)	7 / 278 (2.52%)	0 / 12 (0.00%)
occurrences (all)	17	9	0

Non-serious adverse events	Placebo Switched Over to Pembrolizumab (Second Course)	Placebo Switched Over to Pembrolizumab	

Total subjects affected by non-serious adverse events subjects affected / exposed	0 / 1 (0.00%)	90 / 118 (76.27%)	
Vascular disorders			
Hypotension subjects affected / exposed	0 / 1 (0.00%)	4 / 118 (3.39%)	
occurrences (all)	0	4	
Hypertension subjects affected / exposed	0 / 1 (0.00%)	3 / 118 (2.54%)	
occurrences (all)	0	3	
General disorders and administration site conditions			
Asthenia subjects affected / exposed	0 / 1 (0.00%)	8 / 118 (6.78%)	
occurrences (all)	0	16	
Chest pain subjects affected / exposed	0 / 1 (0.00%)	9 / 118 (7.63%)	
occurrences (all)	0	10	
Fatigue subjects affected / exposed	0 / 1 (0.00%)	15 / 118 (12.71%)	
occurrences (all)	0	15	
Oedema peripheral subjects affected / exposed	0 / 1 (0.00%)	3 / 118 (2.54%)	
occurrences (all)	0	4	
Pyrexia subjects affected / exposed	0 / 1 (0.00%)	5 / 118 (4.24%)	
occurrences (all)	0	7	
Respiratory, thoracic and mediastinal disorders			
Haemoptysis subjects affected / exposed	0 / 1 (0.00%)	12 / 118 (10.17%)	
occurrences (all)	0	14	
Epistaxis subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences (all)	0	0	
Dyspnoea subjects affected / exposed	0 / 1 (0.00%)	15 / 118 (12.71%)	
occurrences (all)	0	15	
Cough			

subjects affected / exposed	0 / 1 (0.00%)	12 / 118 (10.17%)	
occurrences (all)	0	13	
Lung infiltration			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences (all)	0	0	
Hiccups			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences (all)	0	0	
Productive cough			
subjects affected / exposed	0 / 1 (0.00%)	8 / 118 (6.78%)	
occurrences (all)	0	8	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 1 (0.00%)	5 / 118 (4.24%)	
occurrences (all)	0	5	
Anxiety			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences (all)	0	0	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 1 (0.00%)	5 / 118 (4.24%)	
occurrences (all)	0	9	
White blood cell count decreased			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences (all)	0	0	
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 1 (0.00%)	4 / 118 (3.39%)	
occurrences (all)	0	5	
Blood bilirubin increased			
subjects affected / exposed	0 / 1 (0.00%)	3 / 118 (2.54%)	
occurrences (all)	0	6	
Blood creatinine increased			
subjects affected / exposed	0 / 1 (0.00%)	11 / 118 (9.32%)	
occurrences (all)	0	20	
Weight decreased			

subjects affected / exposed	0 / 1 (0.00%)	11 / 118 (9.32%)	
occurrences (all)	0	12	
Platelet count decreased			
subjects affected / exposed	0 / 1 (0.00%)	1 / 118 (0.85%)	
occurrences (all)	0	1	
Neutrophil count decreased			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences (all)	0	0	
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 1 (0.00%)	6 / 118 (5.08%)	
occurrences (all)	0	8	
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 1 (0.00%)	4 / 118 (3.39%)	
occurrences (all)	0	5	
Peripheral sensory neuropathy			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences (all)	0	0	
Paraesthesia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences (all)	0	0	
Neuropathy peripheral			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences (all)	0	0	
Dysgeusia			
subjects affected / exposed	0 / 1 (0.00%)	2 / 118 (1.69%)	
occurrences (all)	0	2	
Headache			
subjects affected / exposed	0 / 1 (0.00%)	4 / 118 (3.39%)	
occurrences (all)	0	9	
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences (all)	0	0	
Leukopenia			

subjects affected / exposed	0 / 1 (0.00%)	1 / 118 (0.85%)	
occurrences (all)	0	1	
Anaemia			
subjects affected / exposed	0 / 1 (0.00%)	17 / 118 (14.41%)	
occurrences (all)	0	26	
Thrombocytopenia			
subjects affected / exposed	0 / 1 (0.00%)	4 / 118 (3.39%)	
occurrences (all)	0	6	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 1 (0.00%)	3 / 118 (2.54%)	
occurrences (all)	0	4	
Vomiting			
subjects affected / exposed	0 / 1 (0.00%)	6 / 118 (5.08%)	
occurrences (all)	0	8	
Stomatitis			
subjects affected / exposed	0 / 1 (0.00%)	2 / 118 (1.69%)	
occurrences (all)	0	2	
Nausea			
subjects affected / exposed	0 / 1 (0.00%)	12 / 118 (10.17%)	
occurrences (all)	0	13	
Dysphagia			
subjects affected / exposed	0 / 1 (0.00%)	3 / 118 (2.54%)	
occurrences (all)	0	3	
Dry mouth			
subjects affected / exposed	0 / 1 (0.00%)	6 / 118 (5.08%)	
occurrences (all)	0	7	
Diarrhoea			
subjects affected / exposed	0 / 1 (0.00%)	16 / 118 (13.56%)	
occurrences (all)	0	22	
Constipation			
subjects affected / exposed	0 / 1 (0.00%)	12 / 118 (10.17%)	
occurrences (all)	0	14	
Hepatobiliary disorders			
Cholestasis			

subjects affected / exposed	0 / 1 (0.00%)	1 / 118 (0.85%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 1 (0.00%)	7 / 118 (5.93%)	
occurrences (all)	0	7	
Pruritus			
subjects affected / exposed	0 / 1 (0.00%)	15 / 118 (12.71%)	
occurrences (all)	0	18	
Dry skin			
subjects affected / exposed	0 / 1 (0.00%)	1 / 118 (0.85%)	
occurrences (all)	0	1	
Alopecia			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences (all)	0	0	
Skin necrosis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences (all)	0	0	
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	0 / 1 (0.00%)	5 / 118 (4.24%)	
occurrences (all)	0	6	
Hyperthyroidism			
subjects affected / exposed	0 / 1 (0.00%)	5 / 118 (4.24%)	
occurrences (all)	0	5	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 1 (0.00%)	10 / 118 (8.47%)	
occurrences (all)	0	13	
Back pain			
subjects affected / exposed	0 / 1 (0.00%)	7 / 118 (5.93%)	
occurrences (all)	0	7	
Myalgia			
subjects affected / exposed	0 / 1 (0.00%)	3 / 118 (2.54%)	
occurrences (all)	0	3	
Pain in extremity			

subjects affected / exposed	0 / 1 (0.00%)	4 / 118 (3.39%)	
occurrences (all)	0	4	
Polyarthritis			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences (all)	0	0	
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 1 (0.00%)	5 / 118 (4.24%)	
occurrences (all)	0	5	
Nasopharyngitis			
subjects affected / exposed	0 / 1 (0.00%)	2 / 118 (1.69%)	
occurrences (all)	0	2	
Pneumonia			
subjects affected / exposed	0 / 1 (0.00%)	5 / 118 (4.24%)	
occurrences (all)	0	6	
Stoma site infection			
subjects affected / exposed	0 / 1 (0.00%)	0 / 118 (0.00%)	
occurrences (all)	0	0	
Upper respiratory tract infection			
subjects affected / exposed	0 / 1 (0.00%)	4 / 118 (3.39%)	
occurrences (all)	0	7	
Urinary tract infection			
subjects affected / exposed	0 / 1 (0.00%)	7 / 118 (5.93%)	
occurrences (all)	0	7	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 1 (0.00%)	9 / 118 (7.63%)	
occurrences (all)	0	11	
Hypercalcaemia			
subjects affected / exposed	0 / 1 (0.00%)	8 / 118 (6.78%)	
occurrences (all)	0	10	
Hyperglycaemia			
subjects affected / exposed	0 / 1 (0.00%)	5 / 118 (4.24%)	
occurrences (all)	0	7	
Hypoalbuminaemia			

subjects affected / exposed	0 / 1 (0.00%)	7 / 118 (5.93%)	
occurrences (all)	0	8	
Hypocalcaemia			
subjects affected / exposed	0 / 1 (0.00%)	4 / 118 (3.39%)	
occurrences (all)	0	5	
Hypokalaemia			
subjects affected / exposed	0 / 1 (0.00%)	8 / 118 (6.78%)	
occurrences (all)	0	13	
Hypomagnesaemia			
subjects affected / exposed	0 / 1 (0.00%)	4 / 118 (3.39%)	
occurrences (all)	0	4	
Hyponatraemia			
subjects affected / exposed	0 / 1 (0.00%)	7 / 118 (5.93%)	
occurrences (all)	0	8	
Hypophosphataemia			
subjects affected / exposed	0 / 1 (0.00%)	7 / 118 (5.93%)	
occurrences (all)	0	9	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
13 October 2017	Amendment 1 (AM1):To attain the necessary number of Chinese participants and events for investigating efficacy and safety in Chinese NSCLC participants, it was proposed to extend the enrollment period beyond the global study.
26 October 2017	AM2: The statistical design was updated to optimize the study for the identification of long-term treatment effect in overall survival (OS) and progression free survival (PFS).
05 December 2017	AM3: The statistical design was updated to optimize the study for the identification of long-term treatment effect in OS and PFS.
29 June 2018	AM4: The statistical design had an update specific to China, aiming to optimize the identification of long-term treatment effects in OS and PFS.
30 July 2018	AM5: Following positive interim results from the global study, participants were provided with the option to discontinue placebo treatment.
30 October 2019	AM6: Due to positive interim results obtained from the China amendment, participants had the opportunity to choose discontinuation of placebo treatment.
22 February 2022	AM7: Incorporating the global amendment, which includes China, language was included regarding the enrollment of participants in a pembrolizumab extension study upon completion of the main study.
06 September 2022	AM8: Including China, the global amendment introduced additional language permitting participants in the crossover phase of the study to be eligible for second-course treatment with pembrolizumab. Furthermore, it allowed participants in the first-course follow-up to be eligible for second-course treatment for a duration longer than 2 years.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported