Clinical trial results:
An Adaptive Phase III, Multicenter, Randomized, Open-Label, Controlled Study of M7824 (bintrafusp alfa) versus Pembrolizumab as a First-line Treatment in Patients with PD-L1 Expressing Advanced Non-small Cell Lung Cancer

Summary

EudraCT number	2018-001517-32
Trial protocol	DE NL BE GR ES IT
Global end of trial date	20 January 2021

Results information

Result version number	v1 (current)
This version publication date	17 October 2024
First version publication date	17 October 2024

Trial information

Trial identification

Sponsor protocol code	MS200647_0037

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03631706
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	EMD Serono Research & Development Institute, Inc
Sponsor organisation address	Frankfurter Strasse 250, Darmstadt, Germany, 64293
Public contact	Communication Center, Merck KGaA,Darmstadt, Germany, +49 6151725200, service@merckgroup.com
Scientific contact	Communication Center, Merck KGaA, Darmstadt, Germany, +49 6151725200, service@emdgroup.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	15 October 2020
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	20 January 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The purpose of the study was to evaluate the efficacy and safety of bintrafusp alfa (M7824) compared with pembrolizumab in subjects with advanced Non-small Cell Lung Cancer (NSCLC) with high Programmed Death-ligand 1 (PD-L1)-tumor expression, with no epidermal growth factor receptor (EGFR) mutation or anaplastic lymphoma kinase (ALK) translocation.

Protection of trial subjects:

Subject protection was ensured by following high medical and ethical standards in accordance with the principles laid down in the Declaration of Helsinki, and that are consistent with Good Clinical Practice and applicable regulations.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	19 October 2018
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 22
Country: Number of subjects enrolled	Canada: 2
Country: Number of subjects enrolled	Spain: 31
Country: Number of subjects enrolled	France: 25
Country: Number of subjects enrolled	Türkiye: 21
Country: Number of subjects enrolled	Belgium: 18
Country: Number of subjects enrolled	Ukraine: 18
Country: Number of subjects enrolled	Italy: 17
Country: Number of subjects enrolled	Netherlands: 12
Country: Number of subjects enrolled	Germany: 7
Country: Number of subjects enrolled	Greece: 4
Country: Number of subjects enrolled	Korea, Republic of: 63
Country: Number of subjects enrolled	China: 19
Country: Number of subjects enrolled	Japan: 16
Country: Number of subjects enrolled	Taiwan: 6
Country: Number of subjects enrolled	Hong Kong: 1
Country: Number of subjects enrolled	Argentina: 11
Country: Number of subjects enrolled	Brazil: 11

Worldwide total number of subjects	304
EEA total number of subjects	114

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)	113
From 65 to 84 years	183
85 years and over	8

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 152 participants were recruited in the study.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	M7824

Arm description:

Subjects received intravenous infusion of M7824 at a dose of 1200 milligrams (mg) once every 2 weeks until confirmed progression of disease, death, unacceptable toxicity, or study withdrawal.

Arm type	Experimental
Investigational medicinal product name	M7824
Investigational medicinal product code	
Other name	Bintrafusp alfa
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Subjects received intravenous infusion of M7824 at a dose of 1200 milligrams (mg) once every 2weeks until confirmed progression of disease, death, unacceptable toxicity, or study withdrawal.

Arm title	Pembrolizumab

Arm description:

Subjects received intravenous infusion of Pembrolizumab at a dose of 200 milligrams (mg) once every 3 weeks until confirmed progression of disease, death, unacceptable toxicity, or study withdrawal.

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

Dosage and administration details:

Subjects received intravenous infusion of Pembrolizumab at a dose of200 milligrams (mg) once every 3 weeks until confirmed progression of disease, death, unacceptable toxicity, or study withdrawal.

Number of subjects in period 1	M7824	Pembrolizumab
Started	152	152
Treated	152	152
Completed	152	152

Baseline characteristics

Reporting groups	
Reporting group title	M7824
Reporting group description:	
Subjects received intravenous infusion of M7824 at a dose of 1200 milligrams (mg) once every 2 weeks until confirmed progression of disease, death, unacceptable toxicity, or study withdrawal.	
Reporting group title	Pembrolizumab
Reporting group description:	
Subjects received intravenous infusion of Pembrolizumab at a dose of 200 milligrams (mg) once every 3 weeks until confirmed progression of disease, death, unacceptable toxicity, or study withdrawal.	

Reporting group values	M7824	Pembrolizumab	Total
Number of subjects	152	152	304
Age categorical Units: Subjects			
Adults (18-64 years)	51	62	113
From 65-84 years	98	85	183
85 years and over	3	5	8
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
Age Continuous Units: Years			
arithmetic mean	67	67	
standard deviation	± 9.56	± 10.17	-
Sex: Female, Male Units: Subjects			
Female	42	36	78
Male	110	116	226
Race/Ethnicity, Customized Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	50	55	105
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	1	0	1
White	91	79	170
Unknown or Not Reported	7	14	21
Other	3	4	7
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	13	11	24
Not Hispanic or Latino	138	138	276
Unknown or Not Reported	1	3	4

End points

End points reporting groups

Reporting group title	M7824

Reporting group description:

Subjects received intravenous infusion of M7824 at a dose of 1200 milligrams (mg) once every 2 weeks until confirmed progression of disease, death, unacceptable toxicity, or study withdrawal.

Reporting group title	Pembrolizumab

Reporting group description:

Subjects received intravenous infusion of Pembrolizumab at a dose of 200 milligrams (mg) once every 3 weeks until confirmed progression of disease, death, unacceptable toxicity, or study withdrawal.

Primary: Progression-Free Survival (PFS) According to Response Evaluation Criteria in Solid Tumors (RECIST Version 1.1) Assessed by Independent Review Committee (IRC)

End point title	Progression-Free Survival (PFS) According to Response Evaluation Criteria in Solid Tumors (RECIST Version 1.1) Assessed by Independent Review Committee (IRC)[1]

End point description:

Progression free survival was defined as the time from randomization of study intervention until the first documentation of disease progression (PD) or death due to any cause, whichever occurred first. PD: At least a 20 percent (%) increase in the sum of the longest diameter (SLD) taking as reference the smallest SLD recorded from baseline or the appearance of 1 or more new lesions. Full analysis set included all subjects who were randomized to study intervention.

End point type	Primary

End point timeframe:

Time from randomization of study drug until the first documentation of PD or death, assessed approximately up to 746 days

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical and comparison analysis were performed in single arm for this endpoint.

End point values	M7824	Pembrolizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	152	152		
Units: months				
median (full range (min-max))	7.0 (0.0 to 19.4)	11.1 (0.0 to 18.0)		

Statistical analyses

No statistical analyses for this end point

Primary: Overall Survival (OS)

End point title	Overall Survival (OS)[2]

End point description:

Overall Survival was defined as the time from randomization of study intervention to the date of death due to any cause. The overall survival was analyzed by using the Kaplan-Meier method. Full analysis set included all subjects who were randomized to study intervention.

End point type	Primary

End point timeframe:

Time from randomization of study drug assessed approximately up to 843 days

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical and comparison analysis were performed in single arm for this endpoint.

End point values	M7824	Pembrolizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	152	152		
Units: months				
median (full range (min-max))	21.1 (0.2 to 22.1)	22.1 (0.1 to 26.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Treatment-Emergent Adverse Events (TEAEs) and Treatment-Related TEAEs According to National Cancer Institute-Common Terminology Criteria for Adverse Events (NCI-CTCAE) version 5.0

End point title	Number of Subjects With Treatment-Emergent Adverse Events (TEAEs) and Treatment-Related TEAEs According to National Cancer Institute-Common Terminology Criteria for Adverse Events (NCI-CTCAE) version 5.0

End point description:

Adverse Event (AE) was defined any untoward medical occurrence in a subject administered with a study drug, which does not necessarily had a causal relationship with this treatment. Serious AE was defined AE that resulted in any of the following outcomes: death; life threatening; persistent/significant disability/incapacity; initial/prolonged inpatient hospitalization; congenital anomaly/birth defect. TEAEs: TEAEs was defined as events with onset date or worsening during the on treatment period. TEAEs included serious AEs and non-serious AEs. Treatment-related TEAEs: reasonably related to the study intervention. Safety analysis set included all subjects who were administered at least one dose of M7824 or Pembrolizumab.

End point type	Secondary

End point timeframe:

Time from first treatment assessed up to approximately 843 days

End point values	M7824	Pembrolizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	151	152		
Units: Subjects				
Subjects with any TEAE	150	145		
Subjects with any serious TEAE	90	61		
Subjects with any Treatment Related TEAEs	124	105		

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (DOR) According to Response Evaluation Criteria in Solid Tumors Version 1.1 (RECIST v1.1) as Assessed by Independent Review Committee (IRC)

End point title	Duration of Response (DOR) According to Response Evaluation Criteria in Solid Tumors Version 1.1 (RECIST v1.1) as Assessed by Independent Review Committee (IRC)

End point description:

DOR was defined for subjects with objective response, as the time from first documentation of objective response (Complete Response [CR] or Partial Response [PR]) to the date of first documentation of progression disease (PD) or death due to any cause, whichever occurred first. CR: Disappearance of all evidence of target and non-target lesions. PR: At least 30% reduction from baseline in the SLD of all lesions. PD: At least a 20 percent (%) increase in the SLD, taking as reference the smallest SLD recorded from baseline or the appearance of 1 or more new lesions. DOR was determined according to RECIST v1.1 and assessed by IRC. Results were calculated based on Kaplan-Meier estimates. Full analysis set included all subjects who were randomized to study intervention.

End point type	Secondary

End point timeframe:

From first documented objective response to PD or death due to any cause, assessed approximately up to 746 days

End point values	M7824	Pembrolizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	71[3]	78[4]		
Units: months				
median (confidence interval 95%)	99999 (99999 to 99999)	99999 (13.5 to 99999)		

Notes:

[3] - 99999 denotes no observation.

[4] - 99999 denotes no observation.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Unconfirmed Best Overall Response According to Response Evaluation Criteria in Solid Tumors Version 1.1 (RECIST v1.1) as Assessed by Independent Review Committee (IRC)

End point title	Percentage of Subjects With Unconfirmed Best Overall Response According to Response Evaluation Criteria in Solid Tumors Version 1.1 (RECIST v1.1) as Assessed by Independent Review Committee (IRC)

End point description:

Percentage of subjects with unconfirmed best overall response that is at least one overall assessment of

complete response (CR) or partial response (PR) reported here. Full analysis set included all subjects who were randomized to study intervention.

End point type	Secondary

End point timeframe:

Time from randomization of study drug until the first documentation of PD or death, assessed approximately up to 746 days

End point values	M7824	Pembrolizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	152	152		
Units: percentage of subjects				
number (confidence interval 95%)	46.7 (38.6 to 55.0)	51.3 (43.1 to 59.5)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Time from first treatment assessed up to approximately 843 days	
Adverse event reporting additional description:	
Safety analysis set included all subjects who were administered at least one dose of M7824 or Pembrolizumab.	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	24.0

Reporting groups	
Reporting group title	M7824
Reporting group description:	
Subjects received intravenous infusion of M7824 at a dose of 1200 milligrams (mg) once every 2 weeks until confirmed progression of disease, death, unacceptable toxicity, or study withdrawal.	
Reporting group title	Pembrolizumab
Reporting group description:	
Subjects received intravenous infusion of Pembrolizumab at a dose of 200 milligrams (mg) once every 3 weeks until confirmed progression of disease, death, unacceptable toxicity, or study withdrawal.	

Serious adverse events	M7824	Pembrolizumab	
Total subjects affected by serious adverse events			
subjects affected / exposed	90 / 151 (59.60%)	61 / 152 (40.13%)	
number of deaths (all causes)	49	43	
number of deaths resulting from adverse events	17	10	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Squamous cell carcinoma of skin			
subjects affected / exposed	5 / 151 (3.31%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	5 / 5	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder cancer			
subjects affected / exposed	1 / 151 (0.66%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder transitional cell carcinoma			
subjects affected / exposed	1 / 151 (0.66%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Cancer pain			
subjects affected / exposed	1 / 151 (0.66%)	1 / 152 (0.66%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Keratoacanthom			
subjects affected / exposed	3 / 151 (1.99%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	3 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastases to central nervous system			
subjects affected / exposed	0 / 151 (0.00%)	2 / 152 (1.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tumour haemorrhage			
subjects affected / exposed	1 / 151 (0.66%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Embolism			
subjects affected / exposed	1 / 151 (0.66%)	2 / 152 (1.32%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic aneurysm			
subjects affected / exposed	1 / 151 (0.66%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Orthostatic hypotension			
subjects affected / exposed	1 / 151 (0.66%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Shock			
subjects affected / exposed	0 / 151 (0.00%)	1 / 152 (0.66%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Hypotension			
subjects affected / exposed	1 / 151 (0.66%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Superior vena cava syndrome			
subjects affected / exposed	1 / 151 (0.66%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Disease progression			
subjects affected / exposed	6 / 151 (3.97%)	7 / 152 (4.61%)	
occurrences causally related to treatment / all	0 / 6	0 / 5	
deaths causally related to treatment / all	0 / 6	0 / 5	
Death			
subjects affected / exposed	1 / 151 (0.66%)	1 / 152 (0.66%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Asthenia			
subjects affected / exposed	0 / 151 (0.00%)	2 / 152 (1.32%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fatigue			
subjects affected / exposed	0 / 151 (0.00%)	1 / 152 (0.66%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperthermia			
subjects affected / exposed	1 / 151 (0.66%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malaise			
subjects affected / exposed	1 / 151 (0.66%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Pyrexia			
subjects affected / exposed	3 / 151 (1.99%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	2 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sudden death			
subjects affected / exposed	1 / 151 (0.66%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
General physical health deterioration			
subjects affected / exposed	1 / 151 (0.66%)	1 / 152 (0.66%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	1 / 151 (0.66%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Interstitial lung disease			
subjects affected / exposed	1 / 151 (0.66%)	1 / 152 (0.66%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute respiratory failure			
subjects affected / exposed	0 / 151 (0.00%)	2 / 152 (1.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Asthma			
subjects affected / exposed	1 / 151 (0.66%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic obstructive pulmonary disease			

subjects affected / exposed	2 / 151 (1.32%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			
subjects affected / exposed	6 / 151 (3.97%)	2 / 152 (1.32%)	
occurrences causally related to treatment / all	0 / 6	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epistaxis			
subjects affected / exposed	1 / 151 (0.66%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemoptysis			
subjects affected / exposed	4 / 151 (2.65%)	1 / 152 (0.66%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Hypoxia			
subjects affected / exposed	2 / 151 (1.32%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			
subjects affected / exposed	1 / 151 (0.66%)	3 / 152 (1.97%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumothorax			
subjects affected / exposed	5 / 151 (3.31%)	1 / 152 (0.66%)	
occurrences causally related to treatment / all	0 / 5	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary haemorrhage			
subjects affected / exposed	3 / 151 (1.99%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	1 / 3	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Respiratory alkalosis			

subjects affected / exposed	0 / 151 (0.00%)	1 / 152 (0.66%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	1 / 151 (0.66%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Stridor			
subjects affected / exposed	0 / 151 (0.00%)	1 / 152 (0.66%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonitis			
subjects affected / exposed	2 / 151 (1.32%)	1 / 152 (0.66%)	
occurrences causally related to treatment / all	2 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Suicide attempt			
subjects affected / exposed	0 / 151 (0.00%)	1 / 152 (0.66%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 151 (0.00%)	1 / 152 (0.66%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 151 (0.00%)	1 / 152 (0.66%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood creatinine increased			
subjects affected / exposed	0 / 151 (0.00%)	1 / 152 (0.66%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Platelet count decreased			
subjects affected / exposed	1 / 151 (0.66%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Troponin increased			
subjects affected / exposed	1 / 151 (0.66%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Weight decreased			
subjects affected / exposed	1 / 151 (0.66%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transaminases increased			
subjects affected / exposed	1 / 151 (0.66%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	1 / 151 (0.66%)	1 / 152 (0.66%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Fractured sacrum			
subjects affected / exposed	1 / 151 (0.66%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hip fracture			
subjects affected / exposed	1 / 151 (0.66%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infusion related reaction			
subjects affected / exposed	2 / 151 (1.32%)	2 / 152 (1.32%)	
occurrences causally related to treatment / all	2 / 2	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

Radiation necrosis			
subjects affected / exposed	0 / 151 (0.00%)	1 / 152 (0.66%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Strangulated incisional hernia			
subjects affected / exposed	1 / 151 (0.66%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thoracic vertebral fracture			
subjects affected / exposed	1 / 151 (0.66%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	2 / 151 (1.32%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Angina pectoris			
subjects affected / exposed	1 / 151 (0.66%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericardial effusion			
subjects affected / exposed	1 / 151 (0.66%)	1 / 152 (0.66%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocarditis			
subjects affected / exposed	0 / 151 (0.00%)	1 / 152 (0.66%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Coronary artery disease			
subjects affected / exposed	1 / 151 (0.66%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiopulmonary failure			

subjects affected / exposed	0 / 151 (0.00%)	1 / 152 (0.66%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac tamponade			
subjects affected / exposed	0 / 151 (0.00%)	1 / 152 (0.66%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure congestive			
subjects affected / exposed	0 / 151 (0.00%)	1 / 152 (0.66%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac arrest			
subjects affected / exposed	0 / 151 (0.00%)	1 / 152 (0.66%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arrhythmia			
subjects affected / exposed	1 / 151 (0.66%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	0 / 151 (0.00%)	1 / 152 (0.66%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Facial paralysis			
subjects affected / exposed	0 / 151 (0.00%)	1 / 152 (0.66%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune-mediated encephalitis			
subjects affected / exposed	0 / 151 (0.00%)	1 / 152 (0.66%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral sensory neuropathy			

subjects affected / exposed	0 / 151 (0.00%)	1 / 152 (0.66%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sciatica			
subjects affected / exposed	1 / 151 (0.66%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral infarction			
subjects affected / exposed	1 / 151 (0.66%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	4 / 151 (2.65%)	1 / 152 (0.66%)	
occurrences causally related to treatment / all	1 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aplastic anaemia			
subjects affected / exposed	1 / 151 (0.66%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Autoimmune haemolytic anaemia			
subjects affected / exposed	1 / 151 (0.66%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune thrombocytopenia			
subjects affected / exposed	1 / 151 (0.66%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Iron deficiency anaemia			
subjects affected / exposed	1 / 151 (0.66%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Agranulocytosis			

subjects affected / exposed	1 / 151 (0.66%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Immune-mediated enterocolitis			
subjects affected / exposed	1 / 151 (0.66%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal haemorrhage			
subjects affected / exposed	1 / 151 (0.66%)	1 / 152 (0.66%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric ulcer haemorrhage			
subjects affected / exposed	1 / 151 (0.66%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenitis			
subjects affected / exposed	1 / 151 (0.66%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	2 / 151 (1.32%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis			
subjects affected / exposed	2 / 151 (1.32%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Autoimmune colitis			
subjects affected / exposed	0 / 151 (0.00%)	1 / 152 (0.66%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain upper			

subjects affected / exposed	2 / 151 (1.32%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain			
subjects affected / exposed	0 / 151 (0.00%)	1 / 152 (0.66%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			
subjects affected / exposed	1 / 151 (0.66%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	1 / 151 (0.66%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper gastrointestinal haemorrhage			
subjects affected / exposed	1 / 151 (0.66%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retroperitoneal haematoma			
subjects affected / exposed	0 / 151 (0.00%)	1 / 152 (0.66%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis			
subjects affected / exposed	1 / 151 (0.66%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal ulcer			
subjects affected / exposed	1 / 151 (0.66%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal obstruction			

subjects affected / exposed	0 / 151 (0.00%)	1 / 152 (0.66%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Bile duct stone			
subjects affected / exposed	1 / 151 (0.66%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis			
subjects affected / exposed	1 / 151 (0.66%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholestasis			
subjects affected / exposed	1 / 151 (0.66%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis			
subjects affected / exposed	2 / 151 (1.32%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatotoxicity			
subjects affected / exposed	1 / 151 (0.66%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Dermatitis			
subjects affected / exposed	0 / 151 (0.00%)	1 / 152 (0.66%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dermatitis bullous			
subjects affected / exposed	1 / 151 (0.66%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Drug eruption			

subjects affected / exposed	1 / 151 (0.66%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eczema			
subjects affected / exposed	1 / 151 (0.66%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Erythema			
subjects affected / exposed	1 / 151 (0.66%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Erythema multiforme			
subjects affected / exposed	1 / 151 (0.66%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lichen planus			
subjects affected / exposed	1 / 151 (0.66%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pemphigoid			
subjects affected / exposed	2 / 151 (1.32%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pruritus			
subjects affected / exposed	1 / 151 (0.66%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin toxicity			
subjects affected / exposed	1 / 151 (0.66%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stevens-Johnson syndrome			

subjects affected / exposed	1 / 151 (0.66%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Toxic skin eruption			
subjects affected / exposed	1 / 151 (0.66%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 151 (0.00%)	2 / 152 (1.32%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune-mediated nephritis			
subjects affected / exposed	1 / 151 (0.66%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephritis			
subjects affected / exposed	0 / 151 (0.00%)	1 / 152 (0.66%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal failure			
subjects affected / exposed	1 / 151 (0.66%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tubulointerstitial nephritis			
subjects affected / exposed	0 / 151 (0.00%)	1 / 152 (0.66%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Adrenal insufficiency			
subjects affected / exposed	1 / 151 (0.66%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adrenocorticotropic hormone			

deficiency			
subjects affected / exposed	0 / 151 (0.00%)	1 / 152 (0.66%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypothyroidism			
subjects affected / exposed	0 / 151 (0.00%)	1 / 152 (0.66%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 151 (0.00%)	1 / 152 (0.66%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fracture pain			
subjects affected / exposed	1 / 151 (0.66%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myopathy			
subjects affected / exposed	1 / 151 (0.66%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myositis			
subjects affected / exposed	0 / 151 (0.00%)	1 / 152 (0.66%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Spondylitis			
subjects affected / exposed	1 / 151 (0.66%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Infections and infestations			
Influenza			
subjects affected / exposed	1 / 151 (0.66%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Infectious pleural effusion			
subjects affected / exposed	0 / 151 (0.00%)	1 / 152 (0.66%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infection			
subjects affected / exposed	1 / 151 (0.66%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Encephalitis			
subjects affected / exposed	1 / 151 (0.66%)	1 / 152 (0.66%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19			
subjects affected / exposed	0 / 151 (0.00%)	1 / 152 (0.66%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	0 / 151 (0.00%)	1 / 152 (0.66%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	1 / 151 (0.66%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacterial sepsis			
subjects affected / exposed	1 / 151 (0.66%)	1 / 152 (0.66%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Lower respiratory tract infection			
subjects affected / exposed	1 / 151 (0.66%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oral candidiasis			

subjects affected / exposed	1 / 151 (0.66%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	9 / 151 (5.96%)	12 / 152 (7.89%)	
occurrences causally related to treatment / all	0 / 9	1 / 12	
deaths causally related to treatment / all	0 / 2	1 / 1	
Pneumonia staphylococcal			
subjects affected / exposed	1 / 151 (0.66%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary sepsis			
subjects affected / exposed	1 / 151 (0.66%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Sepsis			
subjects affected / exposed	0 / 151 (0.00%)	1 / 152 (0.66%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin infection			
subjects affected / exposed	1 / 151 (0.66%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection			
subjects affected / exposed	0 / 151 (0.00%)	1 / 152 (0.66%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	0 / 151 (0.00%)	1 / 152 (0.66%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection bacterial			

subjects affected / exposed	1 / 151 (0.66%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral upper respiratory tract infection			
subjects affected / exposed	1 / 151 (0.66%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	2 / 151 (1.32%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetes mellitus			
subjects affected / exposed	1 / 151 (0.66%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fluid overload			
subjects affected / exposed	1 / 151 (0.66%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoalbuminaemia			
subjects affected / exposed	1 / 151 (0.66%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyponatraemia			
subjects affected / exposed	3 / 151 (1.99%)	0 / 152 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Type 1 diabetes mellitus			
subjects affected / exposed	0 / 151 (0.00%)	1 / 152 (0.66%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypercalcaemia			

subjects affected / exposed	2 / 151 (1.32%)	3 / 152 (1.97%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	M7824	Pembrolizumab	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	140 / 151 (92.72%)	135 / 152 (88.82%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Keratoacanthoma			
subjects affected / exposed	12 / 151 (7.95%)	0 / 152 (0.00%)	
occurrences (all)	12	0	
Vascular disorders			
Hypotension			
subjects affected / exposed	11 / 151 (7.28%)	1 / 152 (0.66%)	
occurrences (all)	11	1	
Hypertension			
subjects affected / exposed	3 / 151 (1.99%)	10 / 152 (6.58%)	
occurrences (all)	3	10	
General disorders and administration site conditions			
Oedema peripheral			
subjects affected / exposed	14 / 151 (9.27%)	13 / 152 (8.55%)	
occurrences (all)	14	13	
Fatigue			
subjects affected / exposed	30 / 151 (19.87%)	26 / 152 (17.11%)	
occurrences (all)	30	26	
Chest pain			
subjects affected / exposed	8 / 151 (5.30%)	6 / 152 (3.95%)	
occurrences (all)	8	6	
Asthenia			
subjects affected / exposed	26 / 151 (17.22%)	30 / 152 (19.74%)	
occurrences (all)	26	30	
Pyrexia			

subjects affected / exposed	28 / 151 (18.54%)	15 / 152 (9.87%)	
occurrences (all)	28	15	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	23 / 151 (15.23%)	22 / 152 (14.47%)	
occurrences (all)	23	22	
Productive cough			
subjects affected / exposed	7 / 151 (4.64%)	11 / 152 (7.24%)	
occurrences (all)	7	11	
Haemoptysis			
subjects affected / exposed	27 / 151 (17.88%)	6 / 152 (3.95%)	
occurrences (all)	27	6	
Epistaxis			
subjects affected / exposed	15 / 151 (9.93%)	2 / 152 (1.32%)	
occurrences (all)	15	2	
Dyspnoea			
subjects affected / exposed	29 / 151 (19.21%)	18 / 152 (11.84%)	
occurrences (all)	29	18	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	16 / 151 (10.60%)	10 / 152 (6.58%)	
occurrences (all)	16	10	
Investigations			
Lipase increased			
subjects affected / exposed	12 / 151 (7.95%)	7 / 152 (4.61%)	
occurrences (all)	12	7	
Gamma-glutamyltransferase increased			
subjects affected / exposed	19 / 151 (12.58%)	16 / 152 (10.53%)	
occurrences (all)	19	16	
Blood thyroid stimulating hormone increased			
subjects affected / exposed	2 / 151 (1.32%)	8 / 152 (5.26%)	
occurrences (all)	2	8	
Blood creatinine increased			
subjects affected / exposed	9 / 151 (5.96%)	13 / 152 (8.55%)	
occurrences (all)	9	13	

Blood bilirubin increased			
subjects affected / exposed	9 / 151 (5.96%)	3 / 152 (1.97%)	
occurrences (all)	9	3	
Blood alkaline phosphatase increased			
subjects affected / exposed	18 / 151 (11.92%)	11 / 152 (7.24%)	
occurrences (all)	18	11	
Aspartate aminotransferase increased			
subjects affected / exposed	23 / 151 (15.23%)	14 / 152 (9.21%)	
occurrences (all)	23	14	
Amylase increased			
subjects affected / exposed	9 / 151 (5.96%)	9 / 152 (5.92%)	
occurrences (all)	9	9	
Alanine aminotransferase increased			
subjects affected / exposed	19 / 151 (12.58%)	16 / 152 (10.53%)	
occurrences (all)	19	16	
Weight decreased			
subjects affected / exposed	10 / 151 (6.62%)	7 / 152 (4.61%)	
occurrences (all)	10	7	
Nervous system disorders			
Dizziness			
subjects affected / exposed	12 / 151 (7.95%)	8 / 152 (5.26%)	
occurrences (all)	12	8	
Headache			
subjects affected / exposed	14 / 151 (9.27%)	14 / 152 (9.21%)	
occurrences (all)	14	14	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	46 / 151 (30.46%)	18 / 152 (11.84%)	
occurrences (all)	46	18	
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	14 / 151 (9.27%)	10 / 152 (6.58%)	
occurrences (all)	14	10	
Nausea			
subjects affected / exposed	19 / 151 (12.58%)	20 / 152 (13.16%)	
occurrences (all)	19	20	

Diarrhoea			
subjects affected / exposed	24 / 151 (15.89%)	24 / 152 (15.79%)	
occurrences (all)	24	24	
Constipation			
subjects affected / exposed	16 / 151 (10.60%)	22 / 152 (14.47%)	
occurrences (all)	16	22	
Abdominal pain upper			
subjects affected / exposed	3 / 151 (1.99%)	8 / 152 (5.26%)	
occurrences (all)	3	8	
Dyspepsia			
subjects affected / exposed	5 / 151 (3.31%)	11 / 152 (7.24%)	
occurrences (all)	5	11	
Skin and subcutaneous tissue disorders			
Rash pruritic			
subjects affected / exposed	8 / 151 (5.30%)	5 / 152 (3.29%)	
occurrences (all)	8	5	
Rash maculo-papular			
subjects affected / exposed	17 / 151 (11.26%)	6 / 152 (3.95%)	
occurrences (all)	17	6	
Rash			
subjects affected / exposed	48 / 151 (31.79%)	25 / 152 (16.45%)	
occurrences (all)	48	25	
Pruritus			
subjects affected / exposed	52 / 151 (34.44%)	42 / 152 (27.63%)	
occurrences (all)	52	42	
Hyperkeratosis			
subjects affected / exposed	8 / 151 (5.30%)	0 / 152 (0.00%)	
occurrences (all)	8	0	
Dry Skin			
subjects affected / exposed	9 / 151 (5.96%)	4 / 152 (2.63%)	
occurrences (all)	9	4	
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	17 / 151 (11.26%)	23 / 152 (15.13%)	
occurrences (all)	17	23	
Hyperthyroidism			

subjects affected / exposed	6 / 151 (3.97%)	10 / 152 (6.58%)	
occurrences (all)	6	10	
Musculoskeletal and connective tissue disorders			
Myalgia			
subjects affected / exposed	11 / 151 (7.28%)	10 / 152 (6.58%)	
occurrences (all)	11	10	
Back pain			
subjects affected / exposed	8 / 151 (5.30%)	13 / 152 (8.55%)	
occurrences (all)	8	13	
Arthralgia			
subjects affected / exposed	20 / 151 (13.25%)	21 / 152 (13.82%)	
occurrences (all)	20	21	
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	11 / 151 (7.28%)	4 / 152 (2.63%)	
occurrences (all)	11	4	
Upper respiratory tract infection			
subjects affected / exposed	9 / 151 (5.96%)	2 / 152 (1.32%)	
occurrences (all)	9	2	
Pneumonia			
subjects affected / exposed	8 / 151 (5.30%)	21 / 152 (13.82%)	
occurrences (all)	8	21	
Metabolism and nutrition disorders			
Hyponatraemia			
subjects affected / exposed	10 / 151 (6.62%)	12 / 152 (7.89%)	
occurrences (all)	10	12	
Hypomagnesaemia			
subjects affected / exposed	4 / 151 (2.65%)	8 / 152 (5.26%)	
occurrences (all)	4	8	
Hypokalaemia			
subjects affected / exposed	5 / 151 (3.31%)	8 / 152 (5.26%)	
occurrences (all)	5	8	
Hypoalbuminaemia			
subjects affected / exposed	16 / 151 (10.60%)	11 / 152 (7.24%)	
occurrences (all)	16	11	
Hyperuricaemia			

subjects affected / exposed	9 / 151 (5.96%)	3 / 152 (1.97%)	
occurrences (all)	9	3	
Hyperglycaemia			
subjects affected / exposed	13 / 151 (8.61%)	10 / 152 (6.58%)	
occurrences (all)	13	10	
Decreased appetite			
subjects affected / exposed	25 / 151 (16.56%)	26 / 152 (17.11%)	
occurrences (all)	25	26	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported