Clinical trial results:
A multicentre randomised phase III trial comparing pembrolizumab versus standard chemotherapy for advanced pre-treated malignant pleural mesothelioma

Summary

EudraCT number	2016-002062-31
Trial protocol	GB ES
Global end of trial date	21 August 2019

Results information

Result version number	v1 (current)
This version publication date	24 September 2021
First version publication date	24 September 2021

Trial information

Trial identification

Sponsor protocol code	ETOP9-15PROMISE-meso

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02991482
WHO universal trial number (UTN)	-
Other trial identifiers	Merck Sharp & Dohme number: 3475-594

Notes:

Sponsors

Sponsor organisation name	European Thoracic Oncology Platform
Sponsor organisation address	Effingerstr. 40, Bern, Germany, 3008
Public contact	ETOP Coordinating Office, ETOP, +41 31 511 94 00, regulatoryoffice@etop-eu.org
Scientific contact	ETOP Coordinating Office, ETOP, +41 31 511 94 00, regulatoryoffice@etop-eu.org

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	21 August 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	20 February 2019
Global end of trial reached?	Yes
Global end of trial date	21 August 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To investigate whether pre-treated mesothelioma patients treated with pembrolizumab have a better outcome in terms of progression-free survival (PFS), as assessed by independent radiological review, compared to standard, institutional-choice chemotherapy (gemcitabine or vinorelbine).

Protection of trial subjects:

Pembrolizumab was withheld for all grade ≥3 (grade 2 for pneumonitis) drug-related toxicities including laboratory abnormalities, and severe or life-threatening adverse events (AEs). Pembrolizumab infusion reaction treatment guidelines were provided. Patients received appropriate supportive care measures as deemed necessary by the treating investigator (treatment delay and supportive care guidelines for pembrolizumab related AEs were also provided). Patients who experienced a recurrence of the same Serious Adverse Event at the same grade or greater with rechallenge of pembrolizumab, discontinued trial medication. At documented disease progression according to RECIST 1.1 criteria, patients in the control arm were allowed to receive pembrolizumab, if they met the cross-over criteria (ECOG PS 0 or 1, absence of progressive tumour at critical anatomical sites requiring urgent alternative medical intervention).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 April 2017
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	Spain: 10
Country: Number of subjects enrolled	United Kingdom: 107
Country: Number of subjects enrolled	Switzerland: 27
Worldwide total number of subjects	144
EEA total number of subjects	117

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	0

months)	
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	41
From 65 to 84 years	103
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

In total, 144 patients were randomised to either Pembrolizumab or to chemotherapy arms in a time duration of 12 months (first patient was randomised in September 2017; last patient was randomised in August 2018).

Pre-assignment

Screening details:

As of February 2019, 151 patients were captured in iBiobank. Of them, 7 were considered ineligible mainly due to life expectancy of <3 months or ECOG PS >1.

Period 1

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

Blinding implementation details:

This is an open-label trial: the patient, the trial site personnel, the sponsor and/or designee are not blinded to treatment.

Arms

Are arms mutually exclusive?	Yes
Arm title	Pembrolizumab

Arm description:

Pembrolizumab, 200 mg fixed dose i.v. on day 1 of every 3-week (±3 days) cycle until progression of disease determined according to RECIST 1.1 criteria or lack of tolerability or until further protocol treatment is declined by the patient, for a maximum of 2 years.

Arm type	Experimental
Investigational medicinal product name	Pembrolizumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Infusion

Dosage and administration details:

Pembrolizumab was administered at 200 mg fixed dose i.v. on day 1 of every 3-week (±3 days) cycle until progression of disease determined according to RECIST 1.1 criteria or lack of tolerability or until further protocol treatment is declined by the patient, for a maximum of 2 years. In case of clinical benefit, with physician and patient agreement, pembrolizumab treatment can continue beyond documented disease progression according to RECIST 1.1 criteria until a maximum of 2 years on pembrolizumab treatment is reached.

Arm title	Chemotherapy

Arm description:

Vinorelbine (p.o.) or vinorelbine (i.v.) or gemcitabine on a per-patient basis prior to randomisation.

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

Dosage and administration details:

Vinorelbine i.v. 30 mg/m2 i.v., day 1 and day 8 of every 3-week (±3 days) cycle. A maximum number of treatment cycles was not mandated.

Investigational medicinal product name	Vinorelbine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Vinorelbine 60/80 mg/m2 p.o., day 1 and day 8 of every 3-week (±3 days) cycle. A maximum number of treatment cycles was not mandated.

Investigational medicinal product name	Gemcitabine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Infusion

Dosage and administration details:

Gemcitabine 1000 mg/m2 i.v., day 1 and day 8 of every 3-week (±3 days) cycle. A maximum number of treatment cycles was not mandated.

Number of subjects in period 1	Pembrolizumab	Chemotherapy
Started	73	71
Completed	8	5
Not completed	65	66
Patient decision	1	1
Physician decision	-	6
Disease progression	56	47
Adverse event, non-fatal	1	6
Death	4	4
Patient feeling too unwell	1	-
Clinical deterioration	1	-
Death prior to study drug initiation	1	-
Worsening of performance status	-	1
Consent withdrawal prior to study drug initiation	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Pembrolizumab
Reporting group description:	
Pembrolizumab, 200 mg fixed dose i.v. on day 1 of every 3-week (±3 days) cycle until progression of disease determined according to RECIST 1.1 criteria or lack of tolerability or until further protocol treatment is declined by the patient, for a maximum of 2 years.	
Reporting group title	Chemotherapy
Reporting group description:	
Vinorelbine (p.o.) or vinorelbine (i.v.) or gemcitabine on a per-patient basis prior to randomisation.	

Reporting group values	Pembrolizumab	Chemotherapy	Total
Number of subjects	73	71	144
Age categorical			
Units: Subjects			
In utero			0
Preterm newborn infants (gestational age < 37 wks)			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)			0
From 65-84 years			0
85 years and over			0
Age continuous			
Units: years			
median	69	71	
full range (min-max)	52 to 83	53 to 83	-
Gender categorical			
Units: Subjects			
Female	15	11	26
Male	58	60	118
Region of enrolment			
Units: Subjects			
United Kingdom	54	53	107
Switzerland	13	14	27
Spain	6	4	10
Histologic subtype			
Units: Subjects			
Epithelioid	66	62	128
Non-epithelioid	7	9	16
Smoking history			
Units: Subjects			
Current	5	4	9
Former (≥100 cigarettes in the whole life)	34	28	62

Never (0-99 cigarettes in the whole life)	33	39	72
Unknown/Missing	1	0	1
ECOG Performance Status			
Of note, although an ECOG performance status (PS) of 0 or 1 was mandatory to be included in the study, one patient was allowed to enter the study with ECOG PS of 2 due to leg braces.			
Units: Subjects			
Zero	21	14	35
One	51	57	108
Two	1	0	1
EORTC score Units: Subjects			
Good prognosis	45	54	99
Poor prognosis	28	17	45
Prior treatment Units: Subjects			
Carboplatin/Pemetrexed	27	27	54
Cisplatin/Pemetrexed	24	22	46
Platinum+/-Pemetrexed+/-Other	13	17	30
Cisplatin/Pemetrexed and Carboplatin/Pemetrexed	7	1	8
Missing	2	4	6
PD-L1 score Units: Subjects			
<1%	36	30	66
1-20%	20	18	38
≥20%	11	14	25
Not evaluable	2	4	6
Not scored	4	5	9

End points

End points reporting groups

Reporting group title	Pembrolizumab
Reporting group description:	
Pembrolizumab, 200 mg fixed dose i.v. on day 1 of every 3-week (±3 days) cycle until progression of disease determined according to RECIST 1.1 criteria or lack of tolerability or until further protocol treatment is declined by the patient, for a maximum of 2 years.	
Reporting group title	Chemotherapy
Reporting group description:	
Vinorelbine (p.o.) or vinorelbine (i.v.) or gemcitabine on a per-patient basis prior to randomisation.	

Primary: Progression Free Survival (PFS) as assessed by independent radiological review

End point title	Progression Free Survival (PFS) as assessed by independent radiological review
End point description:	
PFS is defined as the time from the date of randomization until documented progression by independent radiological review or death, if progression was not documented. If no PFS event was recorded, last tumor assessment date was considered as the censoring date.	
End point type	Primary
End point timeframe:	
Time from randomization of the first patient until database cutoff date for the primary PFS analysis (Sep 2017 - Feb 2019; approximately 1.5 years).	

End point values	Pembrolizumab	Chemotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	73	71		
Units: months				
median (confidence interval 95%)	2.5 (2.1 to 4.2)	3.4 (2.2 to 4.3)		

Statistical analyses

Statistical analysis title	Statistical analysis of the primary endpoint
Comparison groups	Pembrolizumab v Chemotherapy
Number of subjects included in analysis	144
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.76 [1]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.06

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.73
upper limit	1.53

Notes:

[1] - Logrank stratified by histologic subtype

Secondary: Objective response rate by independent radiological review

End point title	Objective response rate by independent radiological review

End point description:

Defined as the best overall response (complete or partial) by independent radiological review, across all assessment time-points from randomization to the end of trial treatment, determined by RECIST 1.1 criteria.

End point type	Secondary

End point timeframe:

Time from randomization of the first patient until termination of trial treatment.

End point values	Pembrolizumab	Chemotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	73	71		
Units: percentage				
number (confidence interval 95%)	21.9 (13.1 to 33.1)	5.6 (1.6 to 13.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Overall survival

End point title	Overall survival

End point description:

Defined as time from the date of randomisation until death from any cause. Censoring will occur at the last follow-up date.

End point type	Secondary

End point timeframe:

Time from randomization of the first patient until database cutoff date for the OS analysis (Sep 2017 - Aug 2019; approximately 2 years).

End point values	Pembrolizumab	Chemotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	73	71		
Units: months				
median (confidence interval 95%)	10.7 (7.6 to 15.0)	12.4 (7.4 to 16.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to treatment failure

End point title	Time to treatment failure

End point description:

Time from from randomisation to discontinuation of treatment for any reason, including progression of disease, treatment toxicity, refusal or death. Censoring will occur at the last follow-up date.

End point type	Secondary

End point timeframe:

Time from randomization of the first patient until database cutoff date for the primary PFS analysis (Sep 2017 - Feb 2019; approximately 1.5 years).

End point values	Pembrolizumab	Chemotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	73	71		
Units: months				
median (confidence interval 95%)	2.8 (2.1 to 4.2)	2.3 (2.1 to 3.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Safety and tolerability

End point title	Safety and tolerability

End point description:

The safety and tolerability of pembrolizumab treatment will be assessed through analysis of the worst grade of toxicity/adverse events according to CTCAE v4.0 criteria observed over the whole treatment period.

End point type	Secondary

End point timeframe:

Adverse events are collected from study treatment initiation to 30 days after treatment is ceased for any reason. Serious adverse events and events of clinical interest are collected within 90 days after last dose of trial treatment.

End point values	Pembrolizumab	Chemotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	72	70		
Units: Subjects				
Any AE	70	65		
Treatment related AE	50	52		
Treatment related AE of grade 3-5	14	18		
Treatment related AE leading to death	1	1		
Treatment realted AE leading to treatment stop	5	5		

Statistical analyses

No statistical analyses for this end point

Secondary: Progression Free Survival (PFS) assessed by investigator

End point title	Progression Free Survival (PFS) assessed by investigator

End point description:

Investigator assessed PFS, from the date of randomisation until documented progression or death, if progression is not documented. Censoring occurs at the last tumor assessment.

End point type	Secondary

End point timeframe:

Time from randomization of the first patient until database cutoff date for the primary PFS analysis (Sep 2017 - Feb 2019; approximately 1.5 years).

End point values	Pembrolizumab	Chemotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	73	71		
Units: Months				
median (confidence interval 95%)	3.5 (2.1 to 4.2)	3.7 (2.2 to 4.3)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All adverse events were collected from study treatment initiation until 30 days after all trial treatment discontinuation. Serious adverse events and events of clinical interest were collected within 90 days after last treatment dose.

Assessment type	Systematic

Dictionary used

Dictionary name	CTCAE
Dictionary version	4.0

Reporting groups

Reporting group title	Pembrolizumab arm (safety cohort)

Reporting group description:

Safety cohort consists of patients that have received at least one dose of trial treatment.

Reporting group title	Chemotherapy (safety cohort)

Reporting group description:

Safety cohort consists of patients that have received at least one dose of trial treatment.

Serious adverse events	Pembrolizumab arm (safety cohort)	Chemotherapy (safety cohort)	
Total subjects affected by serious adverse events			
subjects affected / exposed	27 / 72 (37.50%)	22 / 70 (31.43%)	
number of deaths (all causes)	47	16	
number of deaths resulting from adverse events			
Vascular disorders			
Thromboembolic event			
subjects affected / exposed	0 / 72 (0.00%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Pain			
subjects affected / exposed	0 / 72 (0.00%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malaise			
subjects affected / exposed	1 / 72 (1.39%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			

Cytokine release syndrome			
subjects affected / exposed	1 / 72 (1.39%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypophysitis			
subjects affected / exposed	1 / 72 (1.39%)	0 / 70 (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			
Dyspnea			
subjects affected / exposed	0 / 72 (0.00%)	2 / 70 (2.86%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonitis			
subjects affected / exposed	4 / 72 (5.56%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	4 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Confusion			
subjects affected / exposed	1 / 72 (1.39%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Neutrophil count decreased			
subjects affected / exposed	0 / 72 (0.00%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Alkaline phosphatase increased			
subjects affected / exposed	1 / 72 (1.39%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Cardiac arrest			

subjects affected / exposed	1 / 72 (1.39%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Atrial fibrillation			
subjects affected / exposed	1 / 72 (1.39%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial flutter			
subjects affected / exposed	1 / 72 (1.39%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Heart failure			
subjects affected / exposed	1 / 72 (1.39%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Myocardial infarction			
subjects affected / exposed	0 / 72 (0.00%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Nervous system disorders			
Syncope			
subjects affected / exposed	1 / 72 (1.39%)	0 / 70 (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			
Febrile neutropenia			
subjects affected / exposed	0 / 72 (0.00%)	5 / 70 (7.14%)	
occurrences causally related to treatment / all	0 / 0	4 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	2 / 72 (2.78%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Constipation			
subjects affected / exposed	0 / 72 (0.00%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis			
subjects affected / exposed	2 / 72 (2.78%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhea			
subjects affected / exposed	1 / 72 (1.39%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain			
subjects affected / exposed	1 / 72 (1.39%)	0 / 70 (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			
Rash maculo-papular			
subjects affected / exposed	1 / 72 (1.39%)	0 / 70 (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	2 / 72 (2.78%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Adrenal insufficiency			
subjects affected / exposed	1 / 72 (1.39%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Lung infection			

subjects affected / exposed	4 / 72 (5.56%)	8 / 70 (11.43%)	
occurrences causally related to treatment / all	1 / 4	4 / 8	
deaths causally related to treatment / all	0 / 1	0 / 0	
Bronchial infection			
subjects affected / exposed	2 / 72 (2.78%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	1 / 72 (1.39%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Catheter related infection			
subjects affected / exposed	1 / 72 (1.39%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Otitis media			
subjects affected / exposed	1 / 72 (1.39%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infection NOS			
subjects affected / exposed	0 / 72 (0.00%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory infection			
subjects affected / exposed	1 / 72 (1.39%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Non-neutropaenic infection			
subjects affected / exposed	0 / 72 (0.00%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hypercalcemia			

subjects affected / exposed	1 / 72 (1.39%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperkalemia			
subjects affected / exposed	1 / 72 (1.39%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypokalemia			
subjects affected / exposed	0 / 72 (0.00%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Pembrolizumab arm (safety cohort)	Chemotherapy (safety cohort)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	70 / 72 (97.22%)	65 / 70 (92.86%)	
Investigations			
GGT increased			
subjects affected / exposed	5 / 72 (6.94%)	1 / 70 (1.43%)	
occurrences (all)	5	1	
Weight loss			
subjects affected / exposed	5 / 72 (6.94%)	3 / 70 (4.29%)	
occurrences (all)	5	3	
Alanine aminotransferase increased			
subjects affected / exposed	4 / 72 (5.56%)	4 / 70 (5.71%)	
occurrences (all)	4	4	
Neutrophil count decreased			
subjects affected / exposed	0 / 72 (0.00%)	10 / 70 (14.29%)	
occurrences (all)	0	10	
Nervous system disorders			
Headache			
subjects affected / exposed	4 / 72 (5.56%)	6 / 70 (8.57%)	
occurrences (all)	4	6	
Peripheral sensory neuropathy			

subjects affected / exposed	1 / 72 (1.39%)	4 / 70 (5.71%)	
occurrences (all)	1	4	
Paresthesia			
subjects affected / exposed	1 / 72 (1.39%)	4 / 70 (5.71%)	
occurrences (all)	1	4	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	28 / 72 (38.89%)	32 / 70 (45.71%)	
occurrences (all)	28	32	
Pain			
subjects affected / exposed	19 / 72 (26.39%)	19 / 70 (27.14%)	
occurrences (all)	19	19	
Edema limbs			
subjects affected / exposed	6 / 72 (8.33%)	4 / 70 (5.71%)	
occurrences (all)	6	4	
Flu like symptoms			
subjects affected / exposed	5 / 72 (6.94%)	2 / 70 (2.86%)	
occurrences (all)	5	2	
Fever			
subjects affected / exposed	2 / 72 (2.78%)	5 / 70 (7.14%)	
occurrences (all)	2	5	
Blood and lymphatic system disorders			
Anemia			
subjects affected / exposed	3 / 72 (4.17%)	11 / 70 (15.71%)	
occurrences (all)	3	11	
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	17 / 72 (23.61%)	23 / 70 (32.86%)	
occurrences (all)	17	23	
Nausea			
subjects affected / exposed	16 / 72 (22.22%)	24 / 70 (34.29%)	
occurrences (all)	16	24	
Diarrhea			
subjects affected / exposed	16 / 72 (22.22%)	26 / 70 (37.14%)	
occurrences (all)	16	26	
Vomiting			

subjects affected / exposed	10 / 72 (13.89%)	8 / 70 (11.43%)	
occurrences (all)	10	8	
Mucositis oral			
subjects affected / exposed	5 / 72 (6.94%)	9 / 70 (12.86%)	
occurrences (all)	5	9	
Dry mouth			
subjects affected / exposed	3 / 72 (4.17%)	4 / 70 (5.71%)	
occurrences (all)	3	4	
Abdominal pain			
subjects affected / exposed	2 / 72 (2.78%)	8 / 70 (11.43%)	
occurrences (all)	2	8	
Oral thrush			
subjects affected / exposed	4 / 72 (5.56%)	2 / 70 (2.86%)	
occurrences (all)	4	2	
Respiratory, thoracic and mediastinal disorders			
Dyspnea			
subjects affected / exposed	20 / 72 (27.78%)	10 / 70 (14.29%)	
occurrences (all)	20	10	
Cough			
subjects affected / exposed	16 / 72 (22.22%)	3 / 70 (4.29%)	
occurrences (all)	16	3	
Skin and subcutaneous tissue disorders			
Rash maculo-papular			
subjects affected / exposed	11 / 72 (15.28%)	2 / 70 (2.86%)	
occurrences (all)	11	2	
Dry skin			
subjects affected / exposed	11 / 72 (15.28%)	3 / 70 (4.29%)	
occurrences (all)	11	3	
Pruritus			
subjects affected / exposed	10 / 72 (13.89%)	3 / 70 (4.29%)	
occurrences (all)	10	3	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	8 / 72 (11.11%)	5 / 70 (7.14%)	
occurrences (all)	8	5	
Depression			

subjects affected / exposed	3 / 72 (4.17%)	4 / 70 (5.71%)	
occurrences (all)	3	4	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	7 / 72 (9.72%)	2 / 70 (2.86%)	
occurrences (all)	7	2	
Back pain			
subjects affected / exposed	5 / 72 (6.94%)	3 / 70 (4.29%)	
occurrences (all)	5	3	
Myalgia			
subjects affected / exposed	5 / 72 (6.94%)	0 / 70 (0.00%)	
occurrences (all)	5	0	
Chest wall pain			
subjects affected / exposed	0 / 72 (0.00%)	4 / 70 (5.71%)	
occurrences (all)	0	4	
Infections and infestations			
Lung infection			
subjects affected / exposed	6 / 72 (8.33%)	2 / 70 (2.86%)	
occurrences (all)	6	2	
Urinary tract infection			
subjects affected / exposed	5 / 72 (6.94%)	2 / 70 (2.86%)	
occurrences (all)	5	2	
Bronchial infection			
subjects affected / exposed	4 / 72 (5.56%)	2 / 70 (2.86%)	
occurrences (all)	4	2	
Metabolism and nutrition disorders			
Anorexia			
subjects affected / exposed	12 / 72 (16.67%)	21 / 70 (30.00%)	
occurrences (all)	12	21	
Hypoalbuminemia			
subjects affected / exposed	4 / 72 (5.56%)	2 / 70 (2.86%)	
occurrences (all)	4	2	

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