Clinical trial results:
A PHASE II/III RANDOMIZED STUDY OF PEMBROLIZUMAB IN PATIENTS WITH ADVANCED MALIGNANT PLEURAL MESOTHELIOMA

Summary

EudraCT number	2016-002286-60
Trial protocol	FR GB IT
Global end of trial date	25 July 2024

Results information

Result version number	v1 (current)
This version publication date	26 October 2025
First version publication date	26 October 2025

Trial information

Trial identification

Sponsor protocol code	IND.227

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02784171
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	ISTITUTO NAZIONALE TUMORI - IRCCS FONDAZIONE PASCALE
Sponsor organisation address	Via Mariano Semmola, 52, Napoli, Italy, 80131
Public contact	Unità Sperimentazioni Cliniche, ISTITUTO NAZIONALE TUMORI - IRCCS FONDAZIONE PASCALE, 39 0815903571, m.piccirillo@istitutotumori.na.it
Scientific contact	Unità Sperimentazioni Cliniche, ISTITUTO NAZIONALE TUMORI - IRCCS FONDAZIONE PASCALE, 39 0815903571, m.piccirillo@istitutotumori.na.it
Sponsor organisation name	IFCT
Sponsor organisation address	10 rue de la Grange-Batelière, Paris, France, 75009
Public contact	Contact, IFCT, 33 156811045, operations-cliniques@ifct.fr
Scientific contact	Contact, IFCT, 33 156811045, operations-cliniques@ifct.fr

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	16 September 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	16 September 2022
Global end of trial reached?	Yes
Global end of trial date	25 July 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate whether pembrolizumab, alone or given to patients receiving standard chemotherapy, improves progression free survival in malignant pleural mesothelioma (MPM) compared to standard chemotherapy.

Protection of trial subjects:

Algorithms for management of adverse events were provided in the protocol.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 September 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	Italy: 212
Country: Number of subjects enrolled	Canada: 137
Country: Number of subjects enrolled	France: 91
Worldwide total number of subjects	440
EEA total number of subjects	303

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)	104

From 65 to 84 years	331
85 years and over	5

Subject disposition

Recruitment

Recruitment details:

Between 31Jan2017 and 4Sept2020, 440 patients were enrolled and randomly assigned to chemotherapy (218 patients) or chemotherapy plus pembrolizumab (222 patients). Seven patients were enrolled to the chemotherapy group and immediately withdrew consent or were lost to follow- up and were never treated.

Pre-assignment

Screening details:

Eligible participants were aged 18 years or >, with previously untreated advanced pleural mesothelioma, ECOG PS 0 or 1. Patients were excluded if they had untreated CNS metastases, pneumonitis, glucocorticoids equivalent to more than 10 mg daily of prednisone (within 7 days before the first dose), or with concurrent serious illness or cancer.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Chemo

Arm description:

Cisplatin 75 mg/m² (carboplatin [area under the concentration-time curve 5–6 mg/mL per min] could be substituted) for up to 6 cycles + pemetrexed 500 mg/m² every 3 weeks for up to 6 cycles.

Arm type	Active comparator
Investigational medicinal product name	Ciplatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Intravenous cisplatin 75 mg/m² (carboplatin [area under the concentration-time curve 5–6 mg/mL per min] could be substituted) every 3 weeks for up to 6 cycles.

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

Dosage and administration details:

Intravenous pemetrexed 500 mg/m² every 3 weeks for up to 6 cycles.

Arm title	Chemo+Pembro

Arm description:

Cisplatin 75 mg/m² (carboplatin [area under the concentration-time curve 5–6 mg/mL per min] could be substituted) for up to 6 cycles + pemetrexed 500 mg/m² every 3 weeks for up to 6 cycles + pembrolizumab 200 mg every 3 weeks for up to 2 years.

Arm type	Experimental

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

Dosage and administration details:

Intravenous cisplatin 75 mg/m² (carboplatin [area under the concentration-time curve 5–6 mg/mL per min] could be substituted) every 3 weeks for up to 6 cycles.

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

Dosage and administration details:

Intravenous pemetrexed 500 mg/m² every 3 weeks for up to 6 cycles.

Investigational medicinal product name	Pembrolizumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Intravenous pembrolizumab 200 mg every 3 weeks for up to 2 years.

Number of subjects in period 1	Chemo	Chemo+Pembro
Started	218	222
Completed	211	222
Not completed	7	0
Consent withdrawn by subject	7	-

Baseline characteristics

Reporting groups	
Reporting group title	Chemo
Reporting group description:	
Cisplatin 75 mg/m² (carboplatin [area under the concentration-time curve 5–6 mg/mL per min] could be substituted) for up to 6 cycles + pemetrexed 500 mg/m² every 3 weeks for up to 6 cycles.	
Reporting group title	Chemo+Pembro
Reporting group description:	
Cisplatin 75 mg/m² (carboplatin [area under the concentration-time curve 5–6 mg/mL per min] could be substituted) for up to 6 cycles + pemetrexed 500 mg/m² every 3 weeks for up to 6 cycles + pembrolizumab 200 mg every 3 weeks for up to 2 years.	

Reporting group values	Chemo	Chemo+Pembro	Total
Number of subjects	218	222	440
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	70.9	70.9	
full range (min-max)	28.0 to 88.0	33.2 to 86.7	-
Gender categorical Units: Subjects			
Female	50	57	107
Male	168	165	333
Ethnicity Units: Subjects			
White	172	175	347
Other	1	1	2
Unknown or not reported	45	46	91
Eastern Cooperative Oncology Group performance status score Units: Subjects			
PS 0	105	101	206
PS 1	113	121	234
Previous asbestos exposure Units: Subjects			
Yes	87	98	185
No	131	124	255

Histological subtypes Units: Subjects			
Epithelioid	168	174	342
Mixed or biphasic	27	35	62
Sarcomatoid	21	10	31
Other	2	3	5
European Organisation for Research and Treatment of Cancer prognostic score Units: Subjects			
≤1,27	76	77	153
>1,27	141	145	286
Unknown	1	0	1
PD-L1			
≥ 1% cutoff			
Units: Subjects			
Positive	132	131	263
Negative	63	70	133
Unknown	6	7	13
Not done	17	14	31
Previous smoking history Units: Subjects			
Yes	116	129	245
No	102	93	195
Previous major surgery Units: Subjects			
Yes	24	17	41
No	194	205	399
Previous radiation Units: Subjects			
Yes	16	9	25
No	202	213	415
Previous adjuvant or neoadjuvant chemotherapy Units: Subjects			
Yes	9	3	12
No	209	219	428
Time from first histological diagnosis to random assignment Units: Months			
median	1.8	1.8	
full range (min-max)	0.49 to 169.0	0.26 to 73.4	-

End points

End points reporting groups

Reporting group title	Chemo
Reporting group description:	
Cisplatin 75 mg/m² (carboplatin [area under the concentration-time curve 5–6 mg/mL per min] could be substituted) for up to 6 cycles + pemetrexed 500 mg/m² every 3 weeks for up to 6 cycles.	
Reporting group title	Chemo+Pembro
Reporting group description:	
Cisplatin 75 mg/m² (carboplatin [area under the concentration-time curve 5–6 mg/mL per min] could be substituted) for up to 6 cycles + pemetrexed 500 mg/m² every 3 weeks for up to 6 cycles + pembrolizumab 200 mg every 3 weeks for up to 2 years.	

Primary: Overall Survival (OS)

End point title	Overall Survival (OS)
End point description:	
Time from random assignment to death from any cause. Patients alive at data cutoff were censored at the last day known alive.	
End point type	Primary
End point timeframe:	
Arround 17 months	

End point values	Chemo	Chemo+Pembro		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	211	222		
Units: months				
median (confidence interval 95%)				
All patients	16.1 (13.1 to 18.2)	17.3 (14.4 to 21.3)		
Non-epithelioid histology	8.2 (5.9 to 10.8)	12.3 (8.7 to 21.2)		
Epithelioid histology	18.2 (16.0 to 20.4)	19.8 (16.0 to 22.2)		

Statistical analyses

Statistical analysis title	Primary criteria
Comparison groups	Chemo v Chemo+Pembro

Number of subjects included in analysis	433
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.79
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.64
upper limit	0.94

Secondary: Progression-free survival (PFS)

End point title	Progression-free survival (PFS)

End point description:

Time from the day of random assignment until the first observation of progression or death due to any cause. Patients who were alive without progression were censored at their last date of disease didisease assessment unless definitive therapy had been initiated or two or more consecutive assessments were missed.

End point type	Secondary

End point timeframe:

Arround 17 months

End point values	Chemo	Chemo+Pembro		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	211	222		
Units: months				
median (confidence interval 95%)				
All patients	7.2 (6.8 to 7.7)	7.1 (6.9 to 8.1)		
Non-epithelioid histology	4.5 (4.0 to 6.4)	6.9 (4.5 to 9.7)		
Epithelioid histology	7.4 (7.0 to 8.4)	7.1 (6.9 to 8.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Best overall response rate

End point title	Best overall response rate

End point description:

Complete or partial response; confirmation was not required.
Best overall response as assessed by blinded independent central review, using mRECIST 1.1.

End point type	Secondary

End point timeframe:

Arround 17 months

End point values	Chemo	Chemo+Pembro		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	211	222		
Units: Patients				
Partial response	83	136		
Stable disease or neither complete response nor pr	103	70		
Disease progression	11	9		
Not assessed	13	3		
Baseline images not available	8	2		

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of response

End point title	Duration of response

End point description:

Patients who were alive without progression were censored at their last date of disease assessment unless definitive therapy had been initiated or two or more consecutive assessments were missed.

End point type	Secondary

End point timeframe:

Arround 17 months

End point values	Chemo	Chemo+Pembro		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	211	222		
Units: months				
median (confidence interval 95%)	5.5 (4.2 to 6.0)	5.8 (5.5 to 7.0)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Overall trial (overall period)	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	21

Reporting groups	
Reporting group title	Chemo
Reporting group description: -	
Reporting group title	Chemo + Pembro
Reporting group description: -	

Serious adverse events	Chemo	Chemo + Pembro	
Total subjects affected by serious adverse events			
subjects affected / exposed	38 / 211 (18.01%)	92 / 222 (41.44%)	
number of deaths (all causes)	11	14	
number of deaths resulting from adverse events	2	7	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Neoplasms benign malignant and unspecified (incl cysts and polyps) - Other specify			
subjects affected / exposed	3 / 211 (1.42%)	7 / 222 (3.15%)	
occurrences causally related to treatment / all	0 / 3	0 / 7	
deaths causally related to treatment / all	0 / 3	0 / 5	
Vascular disorders			
Hematoma			
subjects affected / exposed	0 / 211 (0.00%)	1 / 222 (0.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertension			
subjects affected / exposed	0 / 211 (0.00%)	1 / 222 (0.45%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypotension			

subjects affected / exposed	0 / 211 (0.00%)	1 / 222 (0.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thromboembolic event			
subjects affected / exposed	5 / 211 (2.37%)	5 / 222 (2.25%)	
occurrences causally related to treatment / all	1 / 5	1 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vasculitis			
subjects affected / exposed	0 / 211 (0.00%)	2 / 222 (0.90%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Edema limbs			
subjects affected / exposed	1 / 211 (0.47%)	0 / 222 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fever			
subjects affected / exposed	2 / 211 (0.95%)	6 / 222 (2.70%)	
occurrences causally related to treatment / all	1 / 2	1 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Non-cardiac chest pain			
subjects affected / exposed	1 / 211 (0.47%)	0 / 222 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Allergic reaction			
subjects affected / exposed	0 / 211 (0.00%)	1 / 222 (0.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders - Other specify			
subjects affected / exposed	0 / 211 (0.00%)	4 / 222 (1.80%)	
occurrences causally related to treatment / all	0 / 0	4 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	

Social circumstances			
Social circumstances - Other specify			
subjects affected / exposed	0 / 211 (0.00%)	2 / 222 (0.90%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 2	
Reproductive system and breast disorders			
Pelvic pain			
subjects affected / exposed	0 / 211 (0.00%)	1 / 222 (0.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Chylothorax			
subjects affected / exposed	1 / 211 (0.47%)	0 / 222 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cough			
subjects affected / exposed	0 / 211 (0.00%)	1 / 222 (0.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnea			
subjects affected / exposed	4 / 211 (1.90%)	5 / 222 (2.25%)	
occurrences causally related to treatment / all	0 / 4	1 / 5	
deaths causally related to treatment / all	0 / 0	1 / 1	
Pleural effusion			
subjects affected / exposed	2 / 211 (0.95%)	2 / 222 (0.90%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleuritic pain			
subjects affected / exposed	1 / 211 (0.47%)	1 / 222 (0.45%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonitis			

subjects affected / exposed	0 / 211 (0.00%)	8 / 222 (3.60%)	
occurrences causally related to treatment / all	0 / 0	8 / 8	
deaths causally related to treatment / all	0 / 0	1 / 1	
Pneumothorax			
subjects affected / exposed	1 / 211 (0.47%)	2 / 222 (0.90%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary edema			
subjects affected / exposed	0 / 211 (0.00%)	1 / 222 (0.45%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	0 / 211 (0.00%)	1 / 222 (0.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory thoracic and mediastinal disorders - Other specify			
subjects affected / exposed	0 / 211 (0.00%)	1 / 222 (0.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Confusion			
subjects affected / exposed	2 / 211 (0.95%)	0 / 222 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Delirium			
subjects affected / exposed	0 / 211 (0.00%)	2 / 222 (0.90%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 211 (0.00%)	4 / 222 (1.80%)	
occurrences causally related to treatment / all	0 / 0	4 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	

Alkaline phosphatase increased			
subjects affected / exposed	0 / 211 (0.00%)	1 / 222 (0.45%)	
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 / 211 (0.00%)	4 / 222 (1.80%)	
occurrences causally related to treatment / all	0 / 0	4 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Creatinine increased			
subjects affected / exposed	0 / 211 (0.00%)	1 / 222 (0.45%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
GGT increased			
subjects affected / exposed	0 / 211 (0.00%)	1 / 222 (0.45%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lipase increased			
subjects affected / exposed	0 / 211 (0.00%)	2 / 222 (0.90%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Platelet count decreased			
subjects affected / exposed	1 / 211 (0.47%)	5 / 222 (2.25%)	
occurrences causally related to treatment / all	0 / 1	4 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	1 / 211 (0.47%)	0 / 222 (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	0 / 211 (0.00%)	1 / 222 (0.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	1 / 211 (0.47%)	3 / 222 (1.35%)	
occurrences causally related to treatment / all	0 / 1	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial flutter			
subjects affected / exposed	1 / 211 (0.47%)	0 / 222 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac arrest			
subjects affected / exposed	0 / 211 (0.00%)	2 / 222 (0.90%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	1 / 2	
Cardiac disorders - Other specify			
subjects affected / exposed	1 / 211 (0.47%)	0 / 222 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Heart failure			
subjects affected / exposed	0 / 211 (0.00%)	2 / 222 (0.90%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			
subjects affected / exposed	3 / 211 (1.42%)	2 / 222 (0.90%)	
occurrences causally related to treatment / all	2 / 3	0 / 2	
deaths causally related to treatment / all	1 / 1	0 / 1	
Pericardial effusion			
subjects affected / exposed	0 / 211 (0.00%)	1 / 222 (0.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericarditis			
subjects affected / exposed	1 / 211 (0.47%)	0 / 222 (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			

Dysarthria			
subjects affected / exposed	1 / 211 (0.47%)	0 / 222 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Headache			
subjects affected / exposed	1 / 211 (0.47%)	0 / 222 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intracranial hemorrhage			
subjects affected / exposed	1 / 211 (0.47%)	0 / 222 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Myelitis			
subjects affected / exposed	0 / 211 (0.00%)	1 / 222 (0.45%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral motor neuropathy			
subjects affected / exposed	0 / 211 (0.00%)	1 / 222 (0.45%)	
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 / 211 (0.00%)	1 / 222 (0.45%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seizure			
subjects affected / exposed	0 / 211 (0.00%)	1 / 222 (0.45%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tremor			
subjects affected / exposed	0 / 211 (0.00%)	1 / 222 (0.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			

Anemia			
subjects affected / exposed	0 / 211 (0.00%)	7 / 222 (3.15%)	
occurrences causally related to treatment / all	0 / 0	6 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile neutropenia			
subjects affected / exposed	2 / 211 (0.95%)	11 / 222 (4.95%)	
occurrences causally related to treatment / all	2 / 2	9 / 11	
deaths causally related to treatment / all	0 / 0	1 / 1	
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 211 (0.00%)	1 / 222 (0.45%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Blurred vision			
subjects affected / exposed	1 / 211 (0.47%)	0 / 222 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 211 (0.47%)	3 / 222 (1.35%)	
occurrences causally related to treatment / all	0 / 1	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis			
subjects affected / exposed	0 / 211 (0.00%)	4 / 222 (1.80%)	
occurrences causally related to treatment / all	0 / 0	4 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colonic obstruction			
subjects affected / exposed	0 / 211 (0.00%)	1 / 222 (0.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhea			

subjects affected / exposed	3 / 211 (1.42%)	6 / 222 (2.70%)	
occurrences causally related to treatment / all	2 / 3	5 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysphagia			
subjects affected / exposed	1 / 211 (0.47%)	0 / 222 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric ulcer			
subjects affected / exposed	1 / 211 (0.47%)	0 / 222 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			
subjects affected / exposed	1 / 211 (0.47%)	3 / 222 (1.35%)	
occurrences causally related to treatment / all	1 / 1	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis			
subjects affected / exposed	0 / 211 (0.00%)	2 / 222 (0.90%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	0 / 211 (0.00%)	3 / 222 (1.35%)	
occurrences causally related to treatment / all	0 / 0	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Death NOS			
subjects affected / exposed	0 / 211 (0.00%)	1 / 222 (0.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Fatigue			
subjects affected / exposed	3 / 211 (1.42%)	2 / 222 (0.90%)	
occurrences causally related to treatment / all	2 / 3	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Pruritus			

subjects affected / exposed	0 / 211 (0.00%)	1 / 222 (0.45%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Purpura			
subjects affected / exposed	0 / 211 (0.00%)	1 / 222 (0.45%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 211 (0.00%)	3 / 222 (1.35%)	
occurrences causally related to treatment / all	0 / 0	2 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract obstruction			
subjects affected / exposed	0 / 211 (0.00%)	1 / 222 (0.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Adrenal insufficiency			
subjects affected / exposed	0 / 211 (0.00%)	2 / 222 (0.90%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 211 (0.00%)	1 / 222 (0.45%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bone pain			
subjects affected / exposed	0 / 211 (0.00%)	1 / 222 (0.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Joint effusion			
subjects affected / exposed	0 / 211 (0.00%)	1 / 222 (0.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Infections and infestations			
Catheter related infection			
subjects affected / exposed	1 / 211 (0.47%)	3 / 222 (1.35%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterocolitis infectious			
subjects affected / exposed	1 / 211 (0.47%)	0 / 222 (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 - Other specify			
subjects affected / exposed	3 / 211 (1.42%)	3 / 222 (1.35%)	
occurrences causally related to treatment / all	0 / 3	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung infection			
subjects affected / exposed	5 / 211 (2.37%)	9 / 222 (4.05%)	
occurrences causally related to treatment / all	1 / 5	2 / 9	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	2 / 211 (0.95%)	7 / 222 (3.15%)	
occurrences causally related to treatment / all	1 / 2	5 / 7	
deaths causally related to treatment / all	1 / 2	3 / 4	
Skin infection			
subjects affected / exposed	0 / 211 (0.00%)	1 / 222 (0.45%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory infection			
subjects affected / exposed	1 / 211 (0.47%)	0 / 222 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	0 / 211 (0.00%)	3 / 222 (1.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	

Neutrophil count decreased			
subjects affected / exposed	0 / 211 (0.00%)	2 / 222 (0.90%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Anorexia			
subjects affected / exposed	0 / 211 (0.00%)	1 / 222 (0.45%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dehydration			
subjects affected / exposed	2 / 211 (0.95%)	1 / 222 (0.45%)	
occurrences causally related to treatment / all	2 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypercalcemia			
subjects affected / exposed	0 / 211 (0.00%)	1 / 222 (0.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperglycemia			
subjects affected / exposed	0 / 211 (0.00%)	1 / 222 (0.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperkalemia			
subjects affected / exposed	1 / 211 (0.47%)	0 / 222 (0.00%)	
occurrences causally related to treatment / all	0 / 1	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	Chemo	Chemo + Pembro	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	211 / 211 (100.00%)	222 / 222 (100.00%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			

Tumor pain			
subjects affected / exposed	13 / 211 (6.16%)	16 / 222 (7.21%)	
occurrences (all)	13	16	
Vascular disorders			
Hypertension			
subjects affected / exposed	7 / 211 (3.32%)	11 / 222 (4.95%)	
occurrences (all)	7	11	
General disorders and administration site conditions			
Edema limbs			
subjects affected / exposed	20 / 211 (9.48%)	26 / 222 (11.71%)	
occurrences (all)	20	26	
Fatigue			
subjects affected / exposed	141 / 211 (66.82%)	153 / 222 (68.92%)	
occurrences (all)	141	153	
Fever			
subjects affected / exposed	20 / 211 (9.48%)	53 / 222 (23.87%)	
occurrences (all)	20	53	
Flu like symptoms			
subjects affected / exposed	6 / 211 (2.84%)	15 / 222 (6.76%)	
occurrences (all)	6	15	
Non-cardiac chest pain			
subjects affected / exposed	40 / 211 (18.96%)	51 / 222 (22.97%)	
occurrences (all)	40	51	
Pain			
subjects affected / exposed	13 / 211 (6.16%)	14 / 222 (6.31%)	
occurrences (all)	13	14	
Respiratory, thoracic and mediastinal disorders			
Allergic rhinitis			
subjects affected / exposed	6 / 211 (2.84%)	12 / 222 (5.41%)	
occurrences (all)	6	12	
Cough			
subjects affected / exposed	55 / 211 (26.07%)	71 / 222 (31.98%)	
occurrences (all)	55	71	
Dyspnea			
subjects affected / exposed	94 / 211 (44.55%)	119 / 222 (53.60%)	
occurrences (all)	94	119	

Epistaxis			
subjects affected / exposed	7 / 211 (3.32%)	13 / 222 (5.86%)	
occurrences (all)	7	13	
Hiccups			
subjects affected / exposed	5 / 211 (2.37%)	12 / 222 (5.41%)	
occurrences (all)	5	12	
Pleuritic pain			
subjects affected / exposed	12 / 211 (5.69%)	16 / 222 (7.21%)	
occurrences (all)	12	16	
Pneumonitis			
subjects affected / exposed	0 / 211 (0.00%)	12 / 222 (5.41%)	
occurrences (all)	0	12	
Productive cough			
subjects affected / exposed	11 / 211 (5.21%)	12 / 222 (5.41%)	
occurrences (all)	11	12	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	12 / 211 (5.69%)	16 / 222 (7.21%)	
occurrences (all)	12	16	
Insomnia			
subjects affected / exposed	16 / 211 (7.58%)	32 / 222 (14.41%)	
occurrences (all)	16	32	
Nervous system disorders			
Dizziness			
subjects affected / exposed	15 / 211 (7.11%)	24 / 222 (10.81%)	
occurrences (all)	15	24	
Dysgeusia			
subjects affected / exposed	29 / 211 (13.74%)	27 / 222 (12.16%)	
occurrences (all)	29	27	
Headache			
subjects affected / exposed	12 / 211 (5.69%)	21 / 222 (9.46%)	
occurrences (all)	12	21	
Paresthesia			
subjects affected / exposed	12 / 211 (5.69%)	21 / 222 (9.46%)	
occurrences (all)	12	21	
Peripheral sensory neuropathy			

subjects affected / exposed	19 / 211 (9.00%)	31 / 222 (13.96%)	
occurrences (all)	19	31	
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	2 / 211 (0.95%)	13 / 222 (5.86%)	
occurrences (all)	2	13	
Ear and labyrinth disorders			
Hearing impaired			
subjects affected / exposed	13 / 211 (6.16%)	10 / 222 (4.50%)	
occurrences (all)	13	10	
Tinnitus			
subjects affected / exposed	14 / 211 (6.64%)	18 / 222 (8.11%)	
occurrences (all)	14	18	
Eye disorders			
Blurred vision			
subjects affected / exposed	5 / 211 (2.37%)	13 / 222 (5.86%)	
occurrences (all)	5	13	
Conjunctivitis			
subjects affected / exposed	17 / 211 (8.06%)	13 / 222 (5.86%)	
occurrences (all)	17	13	
Dry eye			
subjects affected / exposed	12 / 211 (5.69%)	9 / 222 (4.05%)	
occurrences (all)	12	9	
Watering eyes			
subjects affected / exposed	14 / 211 (6.64%)	29 / 222 (13.06%)	
occurrences (all)	14	29	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	12 / 211 (5.69%)	33 / 222 (14.86%)	
occurrences (all)	12	33	
Constipation			
subjects affected / exposed	55 / 211 (26.07%)	82 / 222 (36.94%)	
occurrences (all)	55	82	
Diarrhea			
subjects affected / exposed	30 / 211 (14.22%)	69 / 222 (31.08%)	
occurrences (all)	30	69	
Dry mouth			

subjects affected / exposed	5 / 211 (2.37%)	12 / 222 (5.41%)	
occurrences (all)	5	12	
Dyspepsia			
subjects affected / exposed	14 / 211 (6.64%)	19 / 222 (8.56%)	
occurrences (all)	14	19	
Dysphagia			
subjects affected / exposed	7 / 211 (3.32%)	11 / 222 (4.95%)	
occurrences (all)	7	11	
Mucositis oral			
subjects affected / exposed	37 / 211 (17.54%)	47 / 222 (21.17%)	
occurrences (all)	37	47	
Nausea			
subjects affected / exposed	100 / 211 (47.39%)	120 / 222 (54.05%)	
occurrences (all)	100	120	
Vomiting			
subjects affected / exposed	35 / 211 (16.59%)	57 / 222 (25.68%)	
occurrences (all)	35	57	
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	6 / 211 (2.84%)	12 / 222 (5.41%)	
occurrences (all)	6	12	
Dry skin			
subjects affected / exposed	3 / 211 (1.42%)	17 / 222 (7.66%)	
occurrences (all)	3	17	
Pruritus			
subjects affected / exposed	12 / 211 (5.69%)	40 / 222 (18.02%)	
occurrences (all)	12	40	
Rash acneiform			
subjects affected / exposed	7 / 211 (3.32%)	12 / 222 (5.41%)	
occurrences (all)	7	12	
Rash maculo-papular			
subjects affected / exposed	18 / 211 (8.53%)	37 / 222 (16.67%)	
occurrences (all)	18	37	
Skin and subcutaneous tissue disorders - Other specify			

subjects affected / exposed	14 / 211 (6.64%)	27 / 222 (12.16%)	
occurrences (all)	14	27	
Thromboembolic event			
subjects affected / exposed	18 / 211 (8.53%)	27 / 222 (12.16%)	
occurrences (all)	18	27	
Renal and urinary disorders			
Urinary tract pain			
subjects affected / exposed	5 / 211 (2.37%)	13 / 222 (5.86%)	
occurrences (all)	5	13	
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	4 / 211 (1.90%)	19 / 222 (8.56%)	
occurrences (all)	4	19	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	3 / 211 (1.42%)	28 / 222 (12.61%)	
occurrences (all)	3	28	
Back pain			
subjects affected / exposed	28 / 211 (13.27%)	36 / 222 (16.22%)	
occurrences (all)	28	36	
Bone pain			
subjects affected / exposed	4 / 211 (1.90%)	11 / 222 (4.95%)	
occurrences (all)	4	11	
Chest wall pain			
subjects affected / exposed	28 / 211 (13.27%)	28 / 222 (12.61%)	
occurrences (all)	28	28	
Myalgia			
subjects affected / exposed	3 / 211 (1.42%)	12 / 222 (5.41%)	
occurrences (all)	3	12	
Pain in extremity			
subjects affected / exposed	12 / 211 (5.69%)	22 / 222 (9.91%)	
occurrences (all)	12	22	
Infections and infestations			
Infections and infestations - Other specify			
subjects affected / exposed	7 / 211 (3.32%)	15 / 222 (6.76%)	
occurrences (all)	7	15	

Lung infection			
subjects affected / exposed	13 / 211 (6.16%)	18 / 222 (8.11%)	
occurrences (all)	13	18	
Upper respiratory infection			
subjects affected / exposed	2 / 211 (0.95%)	11 / 222 (4.95%)	
occurrences (all)	2	11	
Urinary tract infection			
subjects affected / exposed	5 / 211 (2.37%)	17 / 222 (7.66%)	
occurrences (all)	5	17	
Metabolism and nutrition disorders			
Anorexia			
subjects affected / exposed	55 / 211 (26.07%)	65 / 222 (29.28%)	
occurrences (all)	55	65	
Dehydration			
subjects affected / exposed	8 / 211 (3.79%)	13 / 222 (5.86%)	
occurrences (all)	8	13	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
13 December 2016	Changes made to ineligibility criteria regarding pneumonitis following new information received from drug company. The new iRECIST guidelines for immune-oncology trials have been incorporated into the response section of the protocol in order to implement these changes in response assessment.
06 March 2017	Increasingly, Canadian sites are only routinely measuring lipase (and not amylase). Footnote #4 was added to clarify that either lipase or amylase is acceptable. Clarification that the substitution (not only discontinuation) of carboplatin for cisplatin in cases where cisplatin is contraindicated may be allowed on case-by-case basis Central pathology review added as histology is a stratification factor on the study, and epithelioid vs sarcomatoid is difficult to verify based on local pathology reports.
11 April 2018	Study redesigned to a phase 3 study : phase 2 reported separately and all analysed patients were excluded from the phase 3 trial. Clarification added to include future participation of UK sites. Addition of Health Economics Assessment to align with phase III objectives/ design. Patient evaluations updated to include Health Economics, and other updates reflect changes made elsewhere in the protocol with respect to lab and follow up requirements, confirmation of need for iRECIST response evaluations/PD for patients on one of the IO containing arm. Also urinalysis, ECG and electrolytes test frequency has been decreased to ensure consistency with other similar phase III trials; more intensive testing was only planned for the early phase II patients. Section 7.3 updated to reflect additional data/information presented in updated investigators brochures. Changes made to the Dose Modification Guidelines section of the protocol, are largely restructuring (ie to include other new expected events such as myocarditis), in keeping with new information and guidance provided in updated investigator brochures. Statistical analysis updated to reflect phase III objectives and analysis of the increases sample size. Health Utilities Assessment (introduction and copy of questionnaire) now included as new phase III objectives.

03 January 2019	Clarification added to include future participation of France and UK sites. Study schema updated to align with phase III objectives/design. Objectives updated : clarification added to protocol that RECIST 1.1 being used for primary and secondary objective, while iRECIST will be used for exploratory analyses. Standard interim analysis added as now a phase III design. Sample size (n value for phase II vs phase III) clarification added in section 12.3. Treatment and Dose Modification Guidelines updated to reflect additional data/information presented in updated investigators brochure. Changes made to the Dose Modification Guidelines section of the protocol, are largely restructuring (ie discontinue treatment after recurrent grade 3 diarrhea), in keeping with new information and guidance provided in updated investigator brochure. Wording deleted from page 35 as duplicate (monitoring guideline already in Table 2). Update to Eligibility/Ineligibility Criteria : wording updated to reflect CCTG standard of practice. 4.2.11 added to ensure patients receive palliative radiation therapy prior to enrollment, to ensure patient safety with no concurrent radiation on trial and to minimize inevaluability and or the need for censoring for response based endpoints because of other anticancer therapy. Update to Patient Treatment and Follow-up : reference to maximum 6 cycles of chemotherapy added per American Society of Clinical Oncology Clinical Practice Guideline 2018. Clarification added regarding Day 1 re-treatment requirements including steroid taper. Follow-up wording update made to comply with changes to CCTG standard template . Clarification added regarding when central radiology and pathology review will be carried out.
14 April 2020	CCTG to check intent of previous chemo (if any given) prior enrollment to ensure eligibility. CCTG to check extent of previous radiation (if any given to thorax) prior enrollment to ensure eligibility. Clarification added to include LVEF testing for patients with history of hypertension. Rewarding to clarify. Patients with arrhythmias controlled on medication, or with a pacemaker are considered to be eligible. Alignment on updated guidelines from 2018 for Modified RECIST for Mesothelioma. mRecist reference added as clarification. SAE definition with pembrolizumab overdose. Emerging data from other trials with immune checkpoint inhibitors and chemotherapy suggested that a hazard ratio of 0.65 is overly optimistic so revised to align with more commonly used hazard ratio of 0.7. That HR would still demonstrate significant benefit to patients in terms of improvement in survival.
27 October 2020	Clarification that collection of all data , including assessments and questionnaires such as QOL cease when the patients withdraws consent to do so. Patients are having delays for the next cycles when on pembrolizumab alone for minor reduction in CrCL likely related to platinum for earlier (combination) cycles. Provide additional information and ensure compliance with GDPR (General Data Protection Regulation). Clarification that BICR will be used for the primary response based analyses, while CCTG will conduct and publish investigator assessed per their SOPs. Some patients on the study have PD assigned based on new dermal lesions. Updated statistical methodology. Updated statistical methodology to reflect alpha spending for multiple endpoints. Clarification that ORR and PFS will also be analysed in the interim analysis. Change in the item used for pain in QOL (from pain to chest pain) to be consistent with prior Merck analyses.
21 June 2021	PD-L1 as a stratification factor has been removed from the protocol and study objective moved from secondary to exploratory. Dose Modification Guidelines for Drug-Related Adverse Events according to the pembrolizumab product monograph dated 2021Mar04.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Abscence of masking might impact adverse event reporting and decision regarding continuation of therapy. Patients in pembro arm were seen more frequently than those in the chemo arm, this would favour the chemo group for adverse event reporting.

Notes: