Clinical trial results:
A RANDOMIZED, PHASE 2, DOUBLE-BLIND STUDY TO EVALUATE THE EFFICACY OF DOSTARLIMAB PLUS CHEMOTHERAPY VERSUS PEMBROLIZUMAB PLUS CHEMOTHERAPY IN METASTATIC NON-SQUAMOUS NON-SMALL CELL LUNG CANCER

Summary

EudraCT number	2020-002327-11
Trial protocol	DE FR IT RO
Global end of trial date	

Results information

Result version number	v1 (current)
This version publication date	18 August 2023
First version publication date	18 August 2023

Trial information

Trial identification

Sponsor protocol code	213403

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04581824
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	GlaxoSmithKline
Sponsor organisation address	980 Great West Road, Brentford, Middlesex, United Kingdom, TW8 9GS
Public contact	GSK Response Center, GlaxoSmithKline, 1 8664357343, GSKClinicalSupportHD@gsk.com
Scientific contact	GSK Response Center, GlaxoSmithKline, 1 8664357343, GSKClinicalSupportHD@gsk.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	Interim
Date of interim/final analysis	22 September 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	04 August 2022
Global end of trial reached?	No

Notes:

General information about the trial

Main objective of the trial:

To compare the ORR of PD-1 inhibitor dostarlimab vs pembrolizumab administered in combination with chemotherapy as evaluated using RECIST v1.1 based on BICR in participants with metastatic non-squamous NSCLC, without a known EGFR, ALK, ROS-1, or BRAF V600E mutation or other genomic aberration for which a targeted therapy is available, who have received no prior treatment of metastatic disease.

Protection of trial subjects:

Not Applicable

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	19 November 2020
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 40
Country: Number of subjects enrolled	Brazil: 27
Country: Number of subjects enrolled	Chile: 2
Country: Number of subjects enrolled	France: 15
Country: Number of subjects enrolled	Germany: 8
Country: Number of subjects enrolled	Italy: 25
Country: Number of subjects enrolled	Korea, Republic of: 40
Country: Number of subjects enrolled	Poland: 28
Country: Number of subjects enrolled	Romania: 10
Country: Number of subjects enrolled	Spain: 41
Country: Number of subjects enrolled	Taiwan: 4
Country: Number of subjects enrolled	United States: 3
Worldwide total number of subjects	243
EEA total number of subjects	127

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37	0

wk	
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)	122
From 65 to 84 years	121
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

The results presented are till the primary completion date. Data collection is still ongoing and additional results will be provided after study completion.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Dostarlimab + Chemotherapy

Arm description:

Participants with metastatic non-squamous non-small cell lung cancer (NSCLC) received Dostarlimab and Chemotherapy on Day 1 of every 21-day cycle beginning with Cycle 1. The order of administration of the investigational treatments was: dostarlimab first, immediately followed by pemetrexed, followed by cisplatin or carboplatin (Cycles 1 to 4 only). 500 milligram (mg) of Dostarlimab was administered as 30-minute intravenous (IV) infusion of as every three weeks (Q3W). 500 mg/meter^2 (m^2) pemetrexed was administered as a 10-minute IV infusion Q3W. 75 mg/m^2 cisplatin was administered via IV infusion approximately 30 minutes after pemetrexed infusion for Q3W or carboplatin at area under the concentration-time curve (AUC) 5 mg/milliliter/minute Q3W immediately following the pemetrexed infusion.

Arm type	Experimental
Investigational medicinal product name	Cisplatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Cisplatin was administered at 75 mg/m^2 through a 30 minute IV infusion Q3W for 4 cycles (each cycle of 21 days) as per investigator decision.

Investigational medicinal product name	Dostarlimab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Dostarlimab will be administered through a 30 minute infusion at a dose of 500 milligrams (mg) intravenously (IV) every 3 weeks (Q3W) up to a maximum of 35 cycles (each cycle of 21 days).

Investigational medicinal product name	Carboplatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Carboplatin was administered at area under the concentration time curve 5 milligram/milliliters/minute (mg/mL/min) (maximum dose: 750 mg) through a 15 to 60 minute IV infusion Q3W for 4 cycles (each cycle of 21 days) as per investigator decision.

Investigational medicinal product name	Pemetrexed
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Pemetrexed was administered at 500 milligram per meter square (mg/m^2) IV through a 10 minute IV infusion Q3W, up to a maximum of 35 cycles (each cycle of 21 days).

Arm title	Pembrolizumab + Chemotherapy

Arm description:

Participants with metastatic NSCLC received Pembrolizumab and Chemotherapy on Day 1 of every 21-day cycle beginning with Cycle 1. The order of administration of the investigational treatments was: Pembrolizumab first, immediately followed by pemetrexed, followed by cisplatin or carboplatin (Cycles 1 to 4 only). 200 mg of Pembrolizumab was administered as 30-minute IV infusion Q3W. 500 mg/meter^2 (m^2) pemetrexed was administered as a 10-minute IV infusion Q3W. 75 mg/m^2 cisplatin was administered via IV infusion approximately 30 minutes after pemetrexed infusion for Q3W or carboplatin at area under the concentration-time curve (AUC) 5 mg/milliliter/minute Q3W immediately following the pemetrexed infusion.

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

Dosage and administration details:

Pembrolizumab was administered through a 30 minute infusion at a dose of 200 mg Q3W up to a maximum of 35 cycles (each cycle of 21 days).

Investigational medicinal product name	Cisplatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Cisplatin was administered at 75 mg/m^2 through a 30 minute IV infusion Q3W for 4 cycles (each cycle of 21 days) as per investigator decision.

Investigational medicinal product name	Carboplatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Carboplatin was administered at area under the concentration time curve 5 milligram/milliliters/minute (mg/mL/min) (maximum dose: 750 mg) through a 15 to 60 minute IV infusion Q3W for 4 cycles (each cycle of 21 days) as per investigator decision.

Investigational medicinal product name	Pemetrexed
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Pemetrexed was administered at 500 milligram per meter square (mg/m^2) IV through a 10 minute IV infusion Q3W, up to a maximum of 35 cycles (each cycle of 21 days).

Notes:

[1] - The roles blinded appear to be inconsistent with a double blind trial.

Justification: Study design required to keep the Subject and Caregiver blinded

Number of subjects in period 1	Dostarlimab + Chemotherapy	Pembrolizumab + Chemotherapy
Started	121	122
Completed	42	48
Not completed	79	74
Consent withdrawn by subject	3	5
Ongoing	75	69
Lost to follow-up	1	-

Baseline characteristics

Reporting groups

Reporting group title	Dostarlimab + Chemotherapy

Reporting group description:

Participants with metastatic non-squamous non-small cell lung cancer (NSCLC) received Dostarlimab and Chemotherapy on Day 1 of every 21-day cycle beginning with Cycle 1. The order of administration of the investigational treatments was: dostarlimab first, immediately followed by pemetrexed, followed by cisplatin or carboplatin (Cycles 1 to 4 only). 500 milligram (mg) of Dostarlimab was administered as 30-minute intravenous (IV) infusion of as every three weeks (Q3W). 500 mg/meter^2 (m^2) pemetrexed was administered as a 10-minute IV infusion Q3W. 75 mg/m^2 cisplatin was administered via IV infusion approximately 30 minutes after pemetrexed infusion for Q3W or carboplatin at area under the concentration-time curve (AUC) 5 mg/milliliter/minute Q3W immediately following the pemetrexed infusion.

Reporting group title	Pembrolizumab + Chemotherapy

Reporting group description:

Participants with metastatic NSCLC received Pembrolizumab and Chemotherapy on Day 1 of every 21-day cycle beginning with Cycle 1. The order of administration of the investigational treatments was: Pembrolizumab first, immediately followed by pemetrexed, followed by cisplatin or carboplatin (Cycles 1 to 4 only). 200 mg of Pembrolizumab was administered as 30-minute IV infusion Q3W. 500 mg/meter^2 (m^2) pemetrexed was administered as a 10-minute IV infusion Q3W. 75 mg/m^2 cisplatin was administered via IV infusion approximately 30 minutes after pemetrexed infusion for Q3W or carboplatin at area under the concentration-time curve (AUC) 5 mg/milliliter/minute Q3W immediately following the pemetrexed infusion.

Reporting group values	Dostarlimab + Chemotherapy	Pembrolizumab + Chemotherapy	Total
Number of subjects	121	122	243
Age categorical Units: Subjects			
<=18 years	0	0	0
19-64 years	65	57	122
>=65 years	56	65	121
Age continuous Units: years			
median	64.0	65.0	
full range (min-max)	25 to 80	46 to 86	-
Sex: Female, Male Units: Participants			
Female	36	45	81
Male	85	77	162
Race/Ethnicity, Customized Units: Subjects			
American Indian or Alaska Native	1	0	1
Asian	23	21	44
Black or African American	1	3	4
White	87	84	171
Multiple	3	3	6
Not Reported	2	5	7
Unknown	4	6	10
Age, Continuous Units: YEARS			
arithmetic mean	63.4	65.4	
standard deviation	± 9.43	± 8.51	-

End points

End points reporting groups

Reporting group title	Dostarlimab + Chemotherapy

Reporting group description:

Participants with metastatic non-squamous non-small cell lung cancer (NSCLC) received Dostarlimab and Chemotherapy on Day 1 of every 21-day cycle beginning with Cycle 1. The order of administration of the investigational treatments was: dostarlimab first, immediately followed by pemetrexed, followed by cisplatin or carboplatin (Cycles 1 to 4 only). 500 milligram (mg) of Dostarlimab was administered as 30-minute intravenous (IV) infusion of as every three weeks (Q3W). 500 mg/meter^2 (m^2) pemetrexed was administered as a 10-minute IV infusion Q3W. 75 mg/m^2 cisplatin was administered via IV infusion approximately 30 minutes after pemetrexed infusion for Q3W or carboplatin at area under the concentration-time curve (AUC) 5 mg/milliliter/minute Q3W immediately following the pemetrexed infusion.

Reporting group title	Pembrolizumab + Chemotherapy

Reporting group description:

Participants with metastatic NSCLC received Pembrolizumab and Chemotherapy on Day 1 of every 21-day cycle beginning with Cycle 1. The order of administration of the investigational treatments was: Pembrolizumab first, immediately followed by pemetrexed, followed by cisplatin or carboplatin (Cycles 1 to 4 only). 200 mg of Pembrolizumab was administered as 30-minute IV infusion Q3W. 500 mg/meter^2 (m^2) pemetrexed was administered as a 10-minute IV infusion Q3W. 75 mg/m^2 cisplatin was administered via IV infusion approximately 30 minutes after pemetrexed infusion for Q3W or carboplatin at area under the concentration-time curve (AUC) 5 mg/milliliter/minute Q3W immediately following the pemetrexed infusion.

Primary: Overall response rate (ORR)

End point title	Overall response rate (ORR)

End point description:

ORR per response was defined as the percentage of participants who had a confirmed complete response (CR) or confirmed partial response (PR) as their best overall response (BOR) recorded from the date of randomization until disease progression or initiation of new anti-cancer therapy, whichever is earlier based on blinded independent central review (BICR) evaluation criteria in solid tumors (RECIST) version 1.1 (v1.1). CR was defined as disappearance of all target lesions. Any pathological lymph nodes must be <10 millimeter in the short axis. PR was defined as at least a 30% decrease in the sum of the diameters of target lesions, taking as reference the baseline sum diameters (e.g., percent change from baseline).

End point type	Primary

End point timeframe:

Up to approximately 20 months

End point values	Dostarlimab + Chemotherapy	Pembrolizumab + Chemotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	121	122		
Units: Percentage of Participants				
number (confidence interval 95%)	46 (37.2 to 55.6)	37 (28.3 to 46.1)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Dostarlimab + Chemotherapy v Pembrolizumab + Chemotherapy
Number of subjects included in analysis	243
Analysis specification	Pre-specified
Analysis type	
Method	Mantel-Haenszel
Parameter estimate	Difference in Response Rate
Point estimate	9.32
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	1.46
upper limit	17.18

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All cause mortality, non-serious adverse events (Non-SAEs) and serious adverse events (SAEs) were collected from Day 1 and up to approximately 20 months.

Adverse event reporting additional description:

Safety population included all participants who received at least 1 dose of study treatment.

Assessment type	Systematic

Dictionary used

Dictionary name	V 25.0
Dictionary version	25.0

Reporting groups

Reporting group title	Pembrolizumab + Chemotherapy

Reporting group description:

Participants with metastatic NSCLC received Pembrolizumab and Chemotherapy on Day 1 of every 21-day cycle beginning with Cycle 1. The order of administration of the investigational treatments was: Pembrolizumab first, immediately followed by pemetrexed, followed by cisplatin or carboplatin (Cycles 1 to 4 only). 200 mg of Pembrolizumab was administered as 30-minute IV infusion Q3W. 500 mg/meter^2 (m^2) pemetrexed was administered as a 10-minute IV infusion Q3W. 75 mg/m^2 cisplatin was administered via IV infusion approximately 30 minutes after pemetrexed infusion for Q3W or carboplatin at area under the concentration-time curve (AUC) 5 mg/milliliter/minute Q3W immediately following the pemetrexed infusion.

Reporting group title	Dostarlimab + Chemotherapy

Reporting group description:

Participants with metastatic non-squamous non-small cell lung cancer (NSCLC) received Dostarlimab and Chemotherapy on Day 1 of every 21-day cycle beginning with Cycle 1. The order of administration of the investigational treatments was: dostarlimab first, immediately followed by pemetrexed, followed by cisplatin or carboplatin (Cycles 1 to 4 only). 500 milligram (mg) of Dostarlimab was administered as 30-minute intravenous (IV) infusion of as every three weeks (Q3W). 500 mg/meter^2 (m^2) pemetrexed was administered as a 10-minute IV infusion Q3W. 75 mg/m^2 cisplatin was administered via IV infusion approximately 30 minutes after pemetrexed infusion for Q3W or carboplatin at area under the concentration-time curve (AUC) 5 mg/milliliter/minute Q3W immediately following the pemetrexed infusion.

Serious adverse events	Pembrolizumab + Chemotherapy	Dostarlimab + Chemotherapy	
Total subjects affected by serious adverse events			
subjects affected / exposed	55 / 122 (45.08%)	46 / 121 (38.02%)	
number of deaths (all causes)	48	42	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Gastrointestinal neoplasm			
subjects affected / exposed	0 / 122 (0.00%)	1 / 121 (0.83%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cancer pain			

subjects affected / exposed	1 / 122 (0.82%)	0 / 121 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Peripheral artery stenosis			
subjects affected / exposed	1 / 122 (0.82%)	0 / 121 (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			
Asthenia			
subjects affected / exposed	1 / 122 (0.82%)	3 / 121 (2.48%)	
occurrences causally related to treatment / all	1 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest pain			
subjects affected / exposed	1 / 122 (0.82%)	0 / 121 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Disease progression			
subjects affected / exposed	0 / 122 (0.00%)	1 / 121 (0.83%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pain			
subjects affected / exposed	0 / 122 (0.00%)	2 / 121 (1.65%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	4 / 122 (3.28%)	1 / 121 (0.83%)	
occurrences causally related to treatment / all	3 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sudden cardiac death			
subjects affected / exposed	0 / 122 (0.00%)	1 / 121 (0.83%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	

Sudden death			
subjects affected / exposed	0 / 122 (0.00%)	2 / 121 (1.65%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 2	
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 122 (0.00%)	1 / 121 (0.83%)	
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			
Dyspnoea			
subjects affected / exposed	3 / 122 (2.46%)	5 / 121 (4.13%)	
occurrences causally related to treatment / all	1 / 3	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cough			
subjects affected / exposed	1 / 122 (0.82%)	0 / 121 (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 / 122 (1.64%)	2 / 121 (1.65%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aspiration			
subjects affected / exposed	1 / 122 (0.82%)	0 / 121 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Acute respiratory failure			
subjects affected / exposed	1 / 122 (0.82%)	0 / 121 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemoptysis			

subjects affected / exposed	2 / 122 (1.64%)	0 / 121 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoxia			
subjects affected / exposed	1 / 122 (0.82%)	0 / 121 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	2 / 122 (1.64%)	0 / 121 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	1 / 2	0 / 0	
Pulmonary embolism			
subjects affected / exposed	1 / 122 (0.82%)	2 / 121 (1.65%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pneumonitis			
subjects affected / exposed	5 / 122 (4.10%)	3 / 121 (2.48%)	
occurrences causally related to treatment / all	5 / 5	3 / 3	
deaths causally related to treatment / all	0 / 0	1 / 1	
Pleural effusion			
subjects affected / exposed	1 / 122 (0.82%)	4 / 121 (3.31%)	
occurrences causally related to treatment / all	1 / 1	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Interstitial lung disease			
subjects affected / exposed	1 / 122 (0.82%)	0 / 121 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune-mediated lung disease			
subjects affected / exposed	0 / 122 (0.00%)	1 / 121 (0.83%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Pulmonary haemorrhage			

subjects affected / exposed	0 / 122 (0.00%)	1 / 121 (0.83%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Psychiatric disorders			
Confusional state			
subjects affected / exposed	1 / 122 (0.82%)	0 / 121 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 122 (0.82%)	1 / 121 (0.83%)	
occurrences causally related to treatment / all	1 / 1	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 122 (0.00%)	1 / 121 (0.83%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 122 (0.00%)	1 / 121 (0.83%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 122 (0.00%)	1 / 121 (0.83%)	
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	2 / 122 (1.64%)	0 / 121 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General physical condition abnormal			
subjects affected / exposed	1 / 122 (0.82%)	0 / 121 (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			
Gastroenteritis radiation			
subjects affected / exposed	1 / 122 (0.82%)	0 / 121 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lumbar vertebral fracture			
subjects affected / exposed	1 / 122 (0.82%)	0 / 121 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Cardiac arrest			
subjects affected / exposed	2 / 122 (1.64%)	0 / 121 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure			
subjects affected / exposed	1 / 122 (0.82%)	0 / 121 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericardial effusion			
subjects affected / exposed	2 / 122 (1.64%)	1 / 121 (0.83%)	
occurrences causally related to treatment / all	1 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Seizure			
subjects affected / exposed	1 / 122 (0.82%)	0 / 121 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic stroke			
subjects affected / exposed	0 / 122 (0.00%)	1 / 121 (0.83%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhage intracranial			

subjects affected / exposed	1 / 122 (0.82%)	0 / 121 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysarthria			
subjects affected / exposed	1 / 122 (0.82%)	0 / 121 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrovascular accident			
subjects affected / exposed	1 / 122 (0.82%)	0 / 121 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient aphasia			
subjects affected / exposed	1 / 122 (0.82%)	0 / 121 (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	5 / 122 (4.10%)	8 / 121 (6.61%)	
occurrences causally related to treatment / all	6 / 6	9 / 10	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile neutropenia			
subjects affected / exposed	4 / 122 (3.28%)	4 / 121 (3.31%)	
occurrences causally related to treatment / all	4 / 4	3 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancytopenia			
subjects affected / exposed	1 / 122 (0.82%)	0 / 121 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			
subjects affected / exposed	3 / 122 (2.46%)	3 / 121 (2.48%)	
occurrences causally related to treatment / all	3 / 3	3 / 3	
deaths causally related to treatment / all	1 / 1	0 / 0	
Neutropenia			

subjects affected / exposed	3 / 122 (2.46%)	0 / 121 (0.00%)	
occurrences causally related to treatment / all	3 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myelosuppression			
subjects affected / exposed	1 / 122 (0.82%)	0 / 121 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 122 (0.00%)	1 / 121 (0.83%)	
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 / 122 (1.64%)	1 / 121 (0.83%)	
occurrences causally related to treatment / all	2 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Constipation			
subjects affected / exposed	2 / 122 (1.64%)	1 / 121 (0.83%)	
occurrences causally related to treatment / all	2 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	2 / 122 (1.64%)	1 / 121 (0.83%)	
occurrences causally related to treatment / all	2 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysphagia			
subjects affected / exposed	0 / 122 (0.00%)	1 / 121 (0.83%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enteritis			
subjects affected / exposed	0 / 122 (0.00%)	1 / 121 (0.83%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal obstruction			

subjects affected / exposed	0 / 122 (0.00%)	1 / 121 (0.83%)	
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 / 122 (0.82%)	0 / 121 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis acute			
subjects affected / exposed	0 / 122 (0.00%)	1 / 121 (0.83%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	1 / 122 (0.82%)	0 / 121 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Hepatitis			
subjects affected / exposed	0 / 122 (0.00%)	1 / 121 (0.83%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 122 (0.00%)	1 / 121 (0.83%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angioedema			
subjects affected / exposed	0 / 122 (0.00%)	1 / 121 (0.83%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Renal failure			
subjects affected / exposed	0 / 122 (0.00%)	1 / 121 (0.83%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Chronic kidney disease			
subjects affected / exposed	0 / 122 (0.00%)	1 / 121 (0.83%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute kidney injury			
subjects affected / exposed	1 / 122 (0.82%)	0 / 121 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 122 (0.82%)	0 / 121 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Back pain			
subjects affected / exposed	1 / 122 (0.82%)	0 / 121 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bone pain			
subjects affected / exposed	0 / 122 (0.00%)	1 / 121 (0.83%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal chest pain			
subjects affected / exposed	1 / 122 (0.82%)	0 / 121 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain in extremity			
subjects affected / exposed	0 / 122 (0.00%)	1 / 121 (0.83%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Pneumocystis jirovecii pneumonia			
subjects affected / exposed	1 / 122 (0.82%)	1 / 121 (0.83%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	

COVID-19			
subjects affected / exposed	0 / 122 (0.00%)	4 / 121 (3.31%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 1	
COVID-19 pneumonia			
subjects affected / exposed	1 / 122 (0.82%)	0 / 121 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Clostridium difficile infection			
subjects affected / exposed	1 / 122 (0.82%)	0 / 121 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pneumonia			
subjects affected / exposed	12 / 122 (9.84%)	4 / 121 (3.31%)	
occurrences causally related to treatment / all	2 / 12	2 / 4	
deaths causally related to treatment / all	1 / 4	0 / 1	
Pulmonary sepsis			
subjects affected / exposed	0 / 122 (0.00%)	1 / 121 (0.83%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Respiratory tract infection			
subjects affected / exposed	1 / 122 (0.82%)	3 / 121 (2.48%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	2 / 122 (1.64%)	0 / 121 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic shock			
subjects affected / exposed	1 / 122 (0.82%)	2 / 121 (1.65%)	
occurrences causally related to treatment / all	1 / 1	0 / 2	
deaths causally related to treatment / all	1 / 1	0 / 2	
Strongyloidiasis			

subjects affected / exposed	0 / 122 (0.00%)	1 / 121 (0.83%)	
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 / 122 (0.00%)	1 / 121 (0.83%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urosepsis			
subjects affected / exposed	0 / 122 (0.00%)	1 / 121 (0.83%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Viral infection			
subjects affected / exposed	1 / 122 (0.82%)	0 / 121 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Diabetic ketoacidosis			
subjects affected / exposed	1 / 122 (0.82%)	0 / 121 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Decreased appetite			
subjects affected / exposed	1 / 122 (0.82%)	0 / 121 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperglycaemia			
subjects affected / exposed	2 / 122 (1.64%)	0 / 121 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypocalcaemia			
subjects affected / exposed	1 / 122 (0.82%)	0 / 121 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypomagnesaemia			

subjects affected / exposed	1 / 122 (0.82%)	0 / 121 (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	1 / 122 (0.82%)	0 / 121 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dehydration			
subjects affected / exposed	1 / 122 (0.82%)	0 / 121 (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	Pembrolizumab + Chemotherapy	Dostarlimab + Chemotherapy	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	110 / 122 (90.16%)	114 / 121 (94.21%)	
Investigations			
Weight decreased			
subjects affected / exposed	6 / 122 (4.92%)	7 / 121 (5.79%)	
occurrences (all)	6	9	
Platelet count decreased			
subjects affected / exposed	9 / 122 (7.38%)	2 / 121 (1.65%)	
occurrences (all)	17	2	
Blood creatinine increased			
subjects affected / exposed	6 / 122 (4.92%)	13 / 121 (10.74%)	
occurrences (all)	7	15	
Blood alkaline phosphatase increased			
subjects affected / exposed	7 / 122 (5.74%)	5 / 121 (4.13%)	
occurrences (all)	8	6	
Aspartate aminotransferase increased			
subjects affected / exposed	8 / 122 (6.56%)	9 / 121 (7.44%)	
occurrences (all)	13	14	
Alanine aminotransferase increased			

subjects affected / exposed	13 / 122 (10.66%)	11 / 121 (9.09%)	
occurrences (all)	21	14	
Nervous system disorders			
Headache			
subjects affected / exposed	8 / 122 (6.56%)	7 / 121 (5.79%)	
occurrences (all)	9	11	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	57 / 122 (46.72%)	55 / 121 (45.45%)	
occurrences (all)	121	151	
Neutropenia			
subjects affected / exposed	25 / 122 (20.49%)	16 / 121 (13.22%)	
occurrences (all)	36	28	
Thrombocytopenia			
subjects affected / exposed	9 / 122 (7.38%)	13 / 121 (10.74%)	
occurrences (all)	14	28	
General disorders and administration site conditions			
Pain			
subjects affected / exposed	3 / 122 (2.46%)	7 / 121 (5.79%)	
occurrences (all)	3	8	
Oedema peripheral			
subjects affected / exposed	9 / 122 (7.38%)	8 / 121 (6.61%)	
occurrences (all)	11	8	
Mucosal inflammation			
subjects affected / exposed	7 / 122 (5.74%)	7 / 121 (5.79%)	
occurrences (all)	10	8	
Fatigue			
subjects affected / exposed	12 / 122 (9.84%)	14 / 121 (11.57%)	
occurrences (all)	16	26	
Chest pain			
subjects affected / exposed	7 / 122 (5.74%)	3 / 121 (2.48%)	
occurrences (all)	8	3	
Asthenia			
subjects affected / exposed	40 / 122 (32.79%)	38 / 121 (31.40%)	
occurrences (all)	69	74	
Pyrexia			

subjects affected / exposed	12 / 122 (9.84%)	12 / 121 (9.92%)	
occurrences (all)	19	15	
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	14 / 122 (11.48%)	20 / 121 (16.53%)	
occurrences (all)	18	29	
Stomatitis			
subjects affected / exposed	5 / 122 (4.10%)	7 / 121 (5.79%)	
occurrences (all)	5	8	
Nausea			
subjects affected / exposed	29 / 122 (23.77%)	28 / 121 (23.14%)	
occurrences (all)	56	65	
Diarrhoea			
subjects affected / exposed	15 / 122 (12.30%)	15 / 121 (12.40%)	
occurrences (all)	18	21	
Constipation			
subjects affected / exposed	22 / 122 (18.03%)	22 / 121 (18.18%)	
occurrences (all)	27	33	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	19 / 122 (15.57%)	19 / 121 (15.70%)	
occurrences (all)	29	30	
Cough			
subjects affected / exposed	20 / 122 (16.39%)	22 / 121 (18.18%)	
occurrences (all)	25	24	
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	10 / 122 (8.20%)	8 / 121 (6.61%)	
occurrences (all)	10	12	
Rash			
subjects affected / exposed	6 / 122 (4.92%)	15 / 121 (12.40%)	
occurrences (all)	6	15	
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	5 / 122 (4.10%)	10 / 121 (8.26%)	
occurrences (all)	5	12	

Hyperthyroidism			
subjects affected / exposed	2 / 122 (1.64%)	7 / 121 (5.79%)	
occurrences (all)	3	10	
Musculoskeletal and connective tissue disorders			
Musculoskeletal chest pain			
subjects affected / exposed	7 / 122 (5.74%)	3 / 121 (2.48%)	
occurrences (all)	8	3	
Back pain			
subjects affected / exposed	14 / 122 (11.48%)	7 / 121 (5.79%)	
occurrences (all)	15	7	
Arthralgia			
subjects affected / exposed	9 / 122 (7.38%)	7 / 121 (5.79%)	
occurrences (all)	9	11	
Infections and infestations			
Respiratory tract infection			
subjects affected / exposed	9 / 122 (7.38%)	6 / 121 (4.96%)	
occurrences (all)	9	7	
Pneumonia			
subjects affected / exposed	6 / 122 (4.92%)	7 / 121 (5.79%)	
occurrences (all)	6	9	
Metabolism and nutrition disorders			
Hypomagnesaemia			
subjects affected / exposed	8 / 122 (6.56%)	8 / 121 (6.61%)	
occurrences (all)	12	13	
Hyperglycaemia			
subjects affected / exposed	8 / 122 (6.56%)	7 / 121 (5.79%)	
occurrences (all)	10	7	
Decreased appetite			
subjects affected / exposed	16 / 122 (13.11%)	19 / 121 (15.70%)	
occurrences (all)	18	25	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
24 July 2020	Created in response to Health Authority feedback to modify the disease eligibility criterion.
10 September 2020	Created in response to Health Authority feedback to modify the contraception eligibility criterion and the chemotherapy study treatments section to ensure that the protocol instructions take local labeling variability into account regarding chemotherapeutic agents.
17 June 2021	Intended to provide a number of clarifications to aspects of the study conduct.
30 November 2021	Intended to allow better study accessibility to patients and to ensure good enrollment rate by lifting the requirement to completely fill 3 TPS stratification cohorts. Per protocol, patients are stratified into 3 TPS cohorts <1%, 1-49% and >50% PD-L1 expression. Additional minor updates to the management of immunotherapy related AEs were done to align with dostarlimab program.
14 February 2023	Intended to allow a better characterization of study efficacy endpoints.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported