Clinical trial results:
A Randomized, Double-blind, Adaptive, Phase II/III Study of GSK3359609 or Placebo in Combination With Pembrolizumab for First-Line Treatment of PD-L1 Positive Recurrent/Metastatic Head and Neck Squamous Cell Carcinoma

Summary

EudraCT number	2019-002263-99
Trial protocol	NL GB IE SE DE PL DK AT NO HU GR PT ES IT RO
Global end of trial date	20 June 2023

Results information

Result version number	v2 (current)
This version publication date	04 July 2024
First version publication date	12 May 2022
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	209229

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04128696
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	GlaxoSmithKline
Sponsor organisation address	Rue de l'Institut 89, Rixensart, Belgium, B-1330
Public contact	GSK Response Center, GlaxoSmithKline, 044 2089-904466, GSKClinicalSupportHD@gsk.com
Scientific contact	GSK Response Center, GlaxoSmithKline, 044 2089-904466, 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	Final
Date of interim/final analysis	13 July 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	27 April 2021
Global end of trial reached?	Yes
Global end of trial date	20 June 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate if the addition of feladilimab to pembrolizumab as first-line treatment improves the efficacy of pembrolizumab in participants with recurrent or metastatic (R/M) head and neck squamous cell carcinoma/cancer (HNSCC).

Protection of trial subjects:

Not applicable

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	21 November 2019
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	Argentina: 1
Country: Number of subjects enrolled	Australia: 20
Country: Number of subjects enrolled	Brazil: 10
Country: Number of subjects enrolled	Canada: 31
Country: Number of subjects enrolled	China: 16
Country: Number of subjects enrolled	Denmark: 1
Country: Number of subjects enrolled	France: 21
Country: Number of subjects enrolled	Germany: 7
Country: Number of subjects enrolled	Greece: 2
Country: Number of subjects enrolled	Israel: 1
Country: Number of subjects enrolled	Italy: 12
Country: Number of subjects enrolled	Japan: 20
Country: Number of subjects enrolled	Korea, Republic of: 18
Country: Number of subjects enrolled	Mexico: 2
Country: Number of subjects enrolled	Netherlands: 7
Country: Number of subjects enrolled	Norway: 6
Country: Number of subjects enrolled	Poland: 26
Country: Number of subjects enrolled	Portugal: 5
Country: Number of subjects enrolled	Romania: 29
Country: Number of subjects enrolled	Russian Federation: 18
Country: Number of subjects enrolled	Spain: 13

Country: Number of subjects enrolled	Switzerland: 3
Country: Number of subjects enrolled	Taiwan: 6
Country: Number of subjects enrolled	United Kingdom: 15
Country: Number of subjects enrolled	United States: 25
Worldwide total number of subjects	315
EEA total number of subjects	129

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)	174
From 65 to 84 years	138
85 years and over	3

Subject disposition

Recruitment

Recruitment details:

Total of 315 participants with recurrent or metastatic head and neck squamous cell carcinoma/cancer (HNSCC) were enrolled in this study.

Pre-assignment

Screening details:

Recruitment in the study was stopped following review of interim safety and efficacy data by the Independent Data Monitoring Committee, after a pre-specified futility analysis. A Dear Investigator Letter (DIL) was issued to stop screening/randomization of further subjects to the study.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Participants receiving feladilimab and pembrolizumab

Arm description:

Participants were administered feladilimab (GSK3359609-humanized anti-ICOS immunoglobulin G4 [IgG4] monoclonal antibody [mAb]) and pembrolizumab (humanized anti-PD-1 IgG4 mAb) as an intravenous (IV) infusion once every three weeks(Q3W).

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

Dosage and administration details:

Participants were administered feladilimab in combination with pembrolizumab as an intravenous infusion over approximately 30 minutes every Q3W.

Arm title	Participants receiving placebo and pembrolizumab

Arm description:

Participants were administered placebo and pembrolizumab (humanized anti-PD-1 IgG4 mAb) as an IV infusion Q3W.

Arm type	Placebo
Investigational medicinal product name	Placebo+ Pembrolizumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Participants were administered placebo in combination with pembrolizumab as an intravenous infusion over approximately 30 minutes every Q3W.

Number of subjects in period 1	Participants receiving feladilimab and pembrolizumab	Participants receiving placebo and pembrolizumab
Started	158	157
mITT population	157	156
Completed	115	98
Not completed	43	59
Consent withdrawn by subject	12	11
Physician decision	2	3
Lost to follow-up	3	7
Study Closed/Terminated	26	38

Baseline characteristics

Reporting groups	
Reporting group title	Participants receiving feladilimab and pembrolizumab
Reporting group description:	
Participants were administered feladilimab (GSK3359609-humanized anti-ICOS immunoglobulin G4 [IgG4] monoclonal antibody [mAb]) and pembrolizumab (humanized anti-PD-1 IgG4 mAb) as an intravenous (IV) infusion once every three weeks(Q3W).	
Reporting group title	Participants receiving placebo and pembrolizumab
Reporting group description:	
Participants were administered placebo and pembrolizumab (humanized anti-PD-1 IgG4 mAb) as an IV infusion Q3W.	

Reporting group values	Participants receiving feladilimab and pembrolizumab	Participants receiving placebo and pembrolizumab	Total
Number of subjects	158	157	315
Age Categorical Units:			
18-64 years	95	79	174
>=65-84 years	62	76	138
>=85 years	1	2	3
Sex: Female, Male Units: Participants			
Female	29	31	60
Male	129	126	255
Race/Ethnicity, Customized Units: Subjects			
Asian - Central/South Asian Heritage	2	0	2
Asian - East Asian Heritage	19	22	41
Asian - Japanese Heritage	12	7	19
Black or African American	4	2	6
Missing	3	6	9
Mixed White Race	1	1	2
Multiple	1	0	1
White - Arabic/North African Heritage	4	1	5
White - White/Caucasian/European Heritage	111	118	229
Native Hawaiian or Other Pacific Islander	1	0	1

End points

End points reporting groups

Reporting group title	Participants receiving feladilimab and pembrolizumab
Reporting group description:	
Participants were administered feladilimab (GSK3359609-humanized anti-ICOS immunoglobulin G4 [IgG4] monoclonal antibody [mAb]) and pembrolizumab (humanized anti-PD-1 IgG4 mAb) as an intravenous (IV) infusion once every three weeks(Q3W).	
Reporting group title	Participants receiving placebo and pembrolizumab
Reporting group description:	
Participants were administered placebo and pembrolizumab (humanized anti-PD-1 IgG4 mAb) as an IV infusion Q3W.	
Subject analysis set title	Feladilimab + pembrolizumab safety analysis set
Subject analysis set type	Safety analysis
Subject analysis set description:	
All randomized participants who took at least 1 dose of study intervention. Participants were assigned to the actual study intervention group of feladilimab + pembrolizumab if the participant received any dose of feladilimab. Participants were analyzed according to the actual study intervention received.	
Subject analysis set title	Placebo + pembrolizumab safety analysis set
Subject analysis set type	Safety analysis
Subject analysis set description:	
All randomized participants who took at least 1 dose of study intervention. Participants were assigned to the actual study intervention group of feladilimab + pembrolizumab if the participant received any dose of feladilimab. Participants were analyzed according to the actual study intervention received.	
Subject analysis set title	Feladilimab +pembrolizumab mITT analysis set
Subject analysis set type	Modified intention-to-treat
Subject analysis set description:	
All randomized participants whether or not randomized intervention was administered, excluding those who were first dosed or randomized after the date of DIL requesting immediate discontinuation of feladilimab /placebo. This analysis set was based on the study intervention to which the participant was randomized.	
Subject analysis set title	Placebo + pembrolizumab mITT analysis set
Subject analysis set type	Modified intention-to-treat
Subject analysis set description:	
All randomized participants whether or not randomized intervention was administered, excluding those who were first dosed or randomized after the date of DIL requesting immediate discontinuation of feladilimab /placebo. This analysis set was based on the study intervention to which the participant was randomized.	

Primary: Overall survival (OS) in the PD-L1 expression positive (Combined positive score [CPS] ≥1) population

End point title	Overall survival (OS) in the PD-L1 expression positive (Combined positive score [CPS] ≥1) population
End point description:	
OS was defined as the time from the date of randomization to the date of death due to any cause. CPS was defined as the ratio of the combined number of PD-L1 expressing tumor cells and immune cells (lymphocytes and macrophages) to the total number of viable tumor cells. Data for participants in the mITT population with CPS ≥1 are presented here. Kaplan-Meier estimate for the median OS is presented, along with associated 95% confidence interval, estimated using the Brookmeyer-Crowley method. 99999 = The median was not reached at the time of primary completion date and the upper limit of the 95% CI was not calculable from the available data at the time of data cut off.	
End point type	Primary
End point timeframe:	
Up to approximately 16 months	

End point values	Feladilimab +pembrolizumab mITT analysis set	Placebo + pembrolizumab mITT analysis set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	157	156		
Units: Week				
median (confidence interval 95%)	44.1 (35.9 to 99999)	99999 (52.4 to 99999)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

The hazard ratio and 2-sided 95% CI was calculated from the cox regression model with Efron's method of tie handling, a treatment covariate and stratified by PD-L1 expression (CPS ≥20 vs. 1≤ CPS <20) and HPV status (oropharynx HPV positive vs oropharynx HPV negative/unknown and non-oropharynx).

Comparison groups	Feladilimab +pembrolizumab mITT analysis set v Placebo + pembrolizumab mITT analysis set
Number of subjects included in analysis	313
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.973 [1]
Method	Stratified Cox proportional hazard model
Parameter estimate	Hazard ratio (HR)
Point estimate	1.51
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.99
upper limit	2.29

Notes:

[1] - Nominal p-value was calculated based on the one-sided log-rank test, stratified by PD-L1 expression (CPS ≥20 vs. 1≤ CPS <20) and HPV status (oropharynx HPV positive vs oropharynx HPV negative/unknown and non-oropharynx)

Primary: OS in the PD-L1 expression high (CPS ≥20) population

End point title	OS in the PD-L1 expression high (CPS ≥20) population

End point description:

OS was defined as the time from the date of randomization to the date of death due to any cause. CPS was defined as the ratio of the combined number of PD-L1 expressing tumor cells and immune cells (lymphocytes and macrophages) to the total number of viable tumor cells. Data for participants who had a PD-L1 CPS of ≥20 are presented here. Kaplan-Meier estimate for the median OS is presented, along with associated 95% confidence interval, estimated using the Brookmeyer-Crowley method. 99999 = The median was not reached at the time of primary completion date and the upper limit of the 95% CI was not calculable from the available data at the time of data cut off.

End point type	Primary

End point timeframe:

Up to approximately 16 months

End point values	Feladilimab +pembrolizumab mITT analysis set	Placebo + pembrolizumab mITT analysis set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	70	69		
Units: Week				
median (confidence interval 95%)	42.1 (25.4 to 99999)	99999 (52.4 to 99999)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

The hazard ratio and 2-sided 95% CI was calculated from the Cox regression model with Efron's method of tie handling, a treatment covariate and stratified by HPV status (oropharynx HPV positive vs oropharynx HPV negative/unknown and non-oropharynx)

Comparison groups	Feladilimab +pembrolizumab mITT analysis set v Placebo + pembrolizumab mITT analysis set
Number of subjects included in analysis	139
Analysis specification	Pre-specified
Analysis type	
P-value	> 0.999 [2]
Method	Stratified Cox proportional hazard model
Parameter estimate	Hazard ratio (HR)
Point estimate	4.44
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.01
upper limit	9.82

Notes:

[2] - Nominal p-value was calculated based on the one-sided log-rank test, stratified by HPV status (oropharynx HPV positive vs oropharynx HPV negative/unknown and non-oropharynx).

Primary: Progression-free survival (PFS) per Response Evaluation Criteria in Solid Tumors (RECIST) in the PD-L1 CPS ≥1 population

End point title	Progression-free survival (PFS) per Response Evaluation Criteria in Solid Tumors (RECIST) in the PD-L1 CPS ≥1 population

End point description:

PFS per RECIST version (v)1.1 was defined as the time from the date of randomization to the date of first documented disease progression or death due to any cause, whichever occurs first. CPS was defined as the ratio of the combined number of PD-L1 expressing tumor cells and immune cells (lymphocytes and macrophages) to the total number of viable tumor cells. Data for participants in the mITT population with CPS ≥1 are presented here. Kaplan-Meier estimate for the median PFS is presented, along with associated 95% confidence interval, estimated using the Brookmeyer-Crowley method.

End point type	Primary

End point timeframe:

Up to approximately 16 months

End point values	Feladilimab +pembrolizumab mITT analysis set	Placebo + pembrolizumab mITT analysis set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	157	156		
Units: Week				
median (confidence interval 95%)	10.1 (9.1 to 15.0)	16.0 (14.3 to 26.1)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

The hazard ratio and 2-sided 95% CI was calculated from the Cox regression model with Efron's method of tie handling, a treatment covariate and stratified by PD-L1 expression (CPS ≥20 vs. 1≤ CPS <20) and HPV status (oropharynx HPV positive vs oropharynx HPV negative/unknown and non-oropharynx)

Comparison groups	Feladilimab +pembrolizumab mITT analysis set v Placebo + pembrolizumab mITT analysis set
Number of subjects included in analysis	313
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.989 [3]
Method	Stratified Cox proportional hazard model
Parameter estimate	Hazard ratio (HR)
Point estimate	1.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.05
upper limit	1.86

Notes:

[3] - Nominal P-value was calculated based on the one-sided log-rank test, stratified by stratified by PD-L1 expression (CPS ≥20 vs. 1≤ CPS <20) and HPV status (oropharynx HPV positive vs oropharynx HPV negative/unknown and non-oropharynx).

Secondary: PFS per immune-based RECIST (iRECIST) in the PD-L1 CPS ≥1 population

End point title	PFS per immune-based RECIST (iRECIST) in the PD-L1 CPS ≥1 population

End point description:

PFS per iRECIST was defined as the interval of time from the date of randomization to the date of the first documented disease progression confirmed consecutively per iRECIST based on investigator assessment, or death due to any cause, whichever occurs first. Data for participants in the mITT population with CPS ≥1 are presented here. Kaplan-Meier estimate for the median PFS is presented, along with associated 95% confidence interval, estimated using the Brookmeyer-Crowley method.

End point type	Secondary

End point timeframe:

Up to approximately 16 months

End point values	Feladilimab +pembrolizumab mITT analysis set	Placebo + pembrolizumab mITT analysis set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	157	156		
Units: Week				
median (confidence interval 95%)	13.0 (9.1 to 15.0)	21.4 (15.6 to 27.0)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

The hazard ratio and 2-sided 95% CI was calculated from the Cox regression model with Efron's method of tie handling, a treatment covariate and stratified by PD-L1 expression (CPS ≥20 vs. 1≤ CPS <20) and HPV status (oropharynx HPV positive vs oropharynx HPV negative/unknown and non-oropharynx)

Comparison groups	Feladilimab +pembrolizumab mITT analysis set v Placebo + pembrolizumab mITT analysis set
Number of subjects included in analysis	313
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.996 [4]
Method	Stratified Cox proportional hazard model
Parameter estimate	Hazard ratio (HR)
Point estimate	1.48
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.1
upper limit	1.99

Notes:

[4] - Nominal P-value was calculated based on the one-sided log-rank test, stratified by stratified by PD-L1 expression (CPS ≥20 vs. 1≤ CPS <20) and HPV status (oropharynx HPV positive vs oropharynx HPV negative/unknown and non-oropharynx).

Secondary: PFS per RECIST in the PD-L1 CPS ≥20 population

End point title	PFS per RECIST in the PD-L1 CPS ≥20 population

End point description:

PFS per RECIST v1.1 was defined as the time from the date of randomization to the date of first documented disease progression per RECIST v1.1. CPS was defined as the ratio of the combined number of PD-L1 expressing tumor cells and immune cells (lymphocytes and macrophages) to the total number of viable tumor cells. Data for participants who had a PD-L1 CPS of ≥20 are presented here. Kaplan-Meier estimate for the median PFS is presented, along with associated 95% confidence interval, estimated using the Brookmeyer-Crowley method.

End point type	Secondary

End point timeframe:

Up to approximately 16 months

End point values	Feladilimab +pembrolizumab mITT analysis set	Placebo + pembrolizumab mITT analysis set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	70	69		
Units: Week				
median (confidence interval 95%)	13.0 (8.6 to 26.1)	21.1 (15.6 to 32.9)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description:	
The hazard ratio and 2-sided 95% CI was calculated from the Cox regression model with Efron's method of tie handling, a treatment covariate and stratified by HPV status (oropharynx HPV positive vs oropharynx HPV negative/unknown and non-oropharynx)	
Comparison groups	Feladilimab +pembrolizumab mITT analysis set v Placebo + pembrolizumab mITT analysis set
Number of subjects included in analysis	139
Analysis specification	Pre-specified
Analysis type	
Method	Stratified Cox proportional hazard model
Parameter estimate	Hazard ratio (HR)
Point estimate	1.55
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.98
upper limit	2.43

Secondary: PFS per iRECIST (iPFS) in the PD-L1 CPS ≥20 population

End point title	PFS per iRECIST (iPFS) in the PD-L1 CPS ≥20 population
End point description:	
PFS per iRECIST was defined as the interval of time from the date of randomization to the date of the first documented disease progression confirmed consecutively per iRECIST based on investigator assessment, or death due to any cause, whichever occurs first. Data for participants who had a PD-L1 CPS of ≥20 are presented here. Kaplan-Meier estimate for the median PFS is presented, along with associated 95% confidence interval, estimated using the Brookmeyer-Crowley method.	
End point type	Secondary
End point timeframe:	
Up to approximately 16 months	

End point values	Feladilimab +pembrolizumab mITT analysis set	Placebo + pembrolizumab mITT analysis set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	70	69		
Units: Week				
median (confidence interval 95%)	13.1 (8.6 to 26.7)	26.7 (20.1 to 32.9)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

The hazard ratio and 2-sided 95% CI was calculated from the Cox regression model with Efron's method of tie handling, a treatment covariate and stratified by HPV status (oropharynx HPV positive vs oropharynx HPV negative/unknown and non-oropharynx).

Comparison groups	Feladilimab +pembrolizumab mITT analysis set v Placebo + pembrolizumab mITT analysis set
Number of subjects included in analysis	139
Analysis specification	Pre-specified
Analysis type	
Method	Stratified Cox proportional hazard model
Parameter estimate	Hazard ratio (HR)
Point estimate	1.59
Confidence interval	
level	95 %
sides	2-sided
lower limit	1
upper limit	2.53

Secondary: Milestone OS rate at 12 months in the PD-L1 CPS ≥1 population

End point title	Milestone OS rate at 12 months in the PD-L1 CPS ≥1 population

End point description:

Milestone OS rate at 12 months was estimated using the Kaplan-Meier method. Associated 95% confidence intervals are estimated using the Brookmeyer-Crowley method. Data for participants in the mITT population with CPS ≥1 are presented here. CPS was defined as the ratio of the combined number of PD-L1 expressing tumor cells and immune cells (lymphocytes and macrophages) to the total number of viable tumor cells.

End point type	Secondary

End point timeframe:

12 months

End point values	Feladilimab +pembrolizumab mITT analysis set	Placebo + pembrolizumab mITT analysis set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	157	156		
Units: Percentage of Participants				
number (confidence interval 95%)	44 (30 to 58)	68 (57 to 77)		

Statistical analyses

No statistical analyses for this end point

Secondary: Milestone OS rate at 12 months in the PD-L1 CPS ≥20 population

End point title	Milestone OS rate at 12 months in the PD-L1 CPS ≥20 population

End point description:

OS rate at 12 months was estimated using the Kaplan-Meier method. Associated 95% confidence intervals are estimated using the Brookmeyer-Crowley method. CPS was defined as the ratio of the combined number of PD-L1 expressing tumor cells and immune cells (lymphocytes and macrophages) to the total number of viable tumor cells. Data for participants who had a PD-L1 CPS of ≥20 are presented here.

End point type	Secondary

End point timeframe:

12 months

End point values	Feladilimab +pembrolizumab mITT analysis set	Placebo + pembrolizumab mITT analysis set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	70	69		
Units: Percentage of participants				
number (confidence interval 95%)	46 (28 to 63)	88 (76 to 94)		

Statistical analyses

No statistical analyses for this end point

Secondary: Milestone OS rate at 24 months in the PD-L1 CPS ≥20 population

End point title	Milestone OS rate at 24 months in the PD-L1 CPS ≥20 population

End point description:

Milestone OS rate at 24 months was not evaluated. CPS was defined as the ratio of the combined number of PD-L1 expressing tumor cells and immune cells (lymphocytes and macrophages) to the total number of viable tumor cells.

End point type	Secondary

End point timeframe:

24 months

End point values	Feladilimab +pembrolizumab mITT analysis set	Placebo + pembrolizumab mITT analysis set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	0[5]	0[6]		
Units: Percentage of participants				
number (confidence interval 95%)	(to)	(to)		

Notes:

[5] - No participant had follow-up duration exceeding 24 months.

[6] - No participant had follow-up duration exceeding 24 months.

Statistical analyses

No statistical analyses for this end point

Secondary: Milestone OS rate at 24 months in the PD-L1 CPS ≥1 population

End point title	Milestone OS rate at 24 months in the PD-L1 CPS ≥1 population

End point description:

Milestone OS rate at 24 months was not evaluated. CPS was defined as the ratio of the combined number of PD-L1 expressing tumor cells and immune cells (lymphocytes and macrophages) to the total number of viable tumor cells.

End point type	Secondary

End point timeframe:

24 months

End point values	Feladilimab +pembrolizumab mITT analysis set	Placebo + pembrolizumab mITT analysis set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	0[7]	0[8]		
Units: Percentage of participants				
number (confidence interval 95%)	(to)	(to)		

Notes:

[7] - No participant had follow-up duration exceeding 24 months.

[8] - No participant had follow-up duration exceeding 24 months.

Statistical analyses

No statistical analyses for this end point

Secondary: DCR per RECIST v1.1 in the PD-L1 CPS ≥1 population

End point title	DCR per RECIST v1.1 in the PD-L1 CPS ≥1 population

End point description:

DCR per RECIST v1.1 based upon investigator assessment, was defined as the percentage of participants with a best overall response of CR or PR at any time plus stable disease (SD) meeting the minimum time of 15 weeks. A status of SD≥15 weeks will be assigned if the follow-up disease assessment has met the SD criteria at least once after the date of randomization at a minimum of 14 weeks (98 days) considering a one-week visit window. Rate and associated 2-sided 95 percent Exact (Clopper-Pearson) Confidence Intervals are provided for each treatment arm which are unadjusted. CPS was defined as the ratio of the combined number of PD-L1 expressing tumor cells and immune cells (lymphocytes and macrophages) to the total number of viable tumor cells. Data for participants in the mITT population with CPS ≥1 are presented here.

End point type	Secondary

End point timeframe:

Up to approximately 16 months

End point values	Feladilimab +pembrolizumab mITT analysis set	Placebo + pembrolizumab mITT analysis set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	157	156		
Units: Percentage of Participants				
number (confidence interval 95%)	33.1 (25.8 to 41.1)	44.9 (36.9 to 53.0)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

The comparison between treatment groups was based on the stratified Miettinen & Nurminen method with strata weighting by sample size and a single treatment covariate. Stratification factors included PD-L1 expression (CPS ≥20 vs. 1≤ CPS <20) and HPV status (positive vs. negative). Participants with oropharynx HPV negative/unknown and non-oropharyngeal tumors were combined as the HPV negative group.

Comparison groups	Feladilimab +pembrolizumab mITT analysis set v Placebo + pembrolizumab mITT analysis set
Number of subjects included in analysis	313
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in Percentage
Point estimate	-11.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-22.4
upper limit	-1.1

Secondary: ORR per RECIST v1.1 in the PD-L1 CPS ≥20 population

End point title	ORR per RECIST v1.1 in the PD-L1 CPS ≥20 population

End point description:

ORR per RECIST v1.1 was defined as the proportion of the participants who have a CR or PR as the best overall response per RECIST v1.1 based upon investigator assessment. As a randomized double-blind study in which primary endpoints are OS and PFS, the confirmation of CR and PR was not required. Rate and associated 2-sided 95 percent Exact (Clopper-Pearson) Confidence Intervals are provided for each treatment arm which are unadjusted. CPS was defined as the ratio of the combined number of PD-L1 expressing tumor cells and immune cells (lymphocytes and macrophages) to the total number of viable tumor cells. Data for participants who had a PD-L1 CPS of ≥20 are presented here.

End point type	Secondary

End point timeframe:

Up to approximately 16 months

End point values	Feladilimab +pembrolizumab mITT analysis set	Placebo + pembrolizumab mITT analysis set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	70	69		
Units: Percentage of Participants				
number (confidence interval 95%)	20.0 (11.4 to 31.3)	33.3 (22.4 to 45.7)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

The comparison between treatment groups was based on the stratified Miettinen & Nurminen method with strata weighting by sample size and a single treatment covariate. Stratification factors included HPV status (positive vs. negative). Participants with oropharynx HPV negative/unknown and non-oropharyngeal tumors were combined as the HPV negative group.

Comparison groups	Feladilimab +pembrolizumab mITT analysis set v Placebo + pembrolizumab mITT analysis set
Number of subjects included in analysis	139
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in Percentage
Point estimate	-13.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-27.8
upper limit	1.5

Secondary: ORR per RECIST v1.1 in the PD-L1 CPS ≥1 population

End point title	ORR per RECIST v1.1 in the PD-L1 CPS ≥1 population

End point description:

ORR per RECIST v1.1 was defined as the proportion of the participants who have a complete response (CR) or partial response (PR) as the best overall response per RECIST v1.1 based upon investigator

assessment. As a randomized double-blind study in which primary endpoints are OS and PFS, the confirmation of CR and PR was not required. Rate and associated 2-sided 95 percent Exact (Clopper-Pearson) Confidence Intervals are provided for each treatment arm which are unadjusted. CPS was defined as the ratio of the combined number of PD-L1 expressing tumor cells and immune cells (lymphocytes and macrophages) to the total number of viable tumor cells. Data for participants in the mITT population with CPS ≥1 are presented here.

End point type	Secondary

End point timeframe:

Up to approximately 16 months

End point values	Feladilimab +pembrolizumab mITT analysis set	Placebo + pembrolizumab mITT analysis set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	157	156		
Units: Percentage of Participants				
number (confidence interval 95%)	19.7 (13.8 to 26.8)	25.0 (18.4 to 32.6)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

The comparison between the treatment groups was based on the stratified Miettinen & Nurminen method with strata weighting by sample size and a single treatment covariate. Stratification factors included PD-L1 expression (CPS ≥20 vs. 1≤ CPS <20) and HPV status (positive vs. negative). Participants with oropharynx HPV negative/unknown and non-oropharyngeal tumors were combined as the HPV negative group.

Comparison groups	Feladilimab +pembrolizumab mITT analysis set v Placebo + pembrolizumab mITT analysis set
Number of subjects included in analysis	313
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in Percentage
Point estimate	-5.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-14.6
upper limit	4

Secondary: Number of participants with any adverse events (AEs) and serious adverse events (SAEs)

End point title	Number of participants with any adverse events (AEs) and serious adverse events (SAEs)

End point description:

An AE was defined as any untoward medical occurrence in a clinical study participant, temporally associated with the use of a study intervention, whether or not considered related to the study

intervention. An SAE was defined as any untoward medical occurrence that, at any dose results in death, is life-threatening, requires inpatient hospitalization or prolongation of existing hospitalization, results in persistent disability/incapacity, is a congenital anomaly/birth defect, any other situation such as important medical events according to medical or scientific judgement.

End point type	Secondary

End point timeframe:

Up to approximately 43 months

End point values	Feladilimab + pembrolizumab safety analysis set	Placebo + pembrolizumab safety analysis set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	159	156		
Units: Participants				
Any AE	150	145		
Any SAE	52	53		

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of response (DoR) per RECIST v1.1 in the PD-L1 CPS ≥1 population

End point title	Duration of response (DoR) per RECIST v1.1 in the PD-L1 CPS ≥1 population

End point description:

DoR per RECIST v1.1 is defined as the time from first documented evidence of CR or PR until first documented disease progression per RECIST v1.1 based upon investigator assessment or death due to any cause, whichever occurs first, among participants who demonstrated CR or PR as the best overall response per RECIST v1.1. Kaplan-Meier estimate for the median DoR is presented, along with associated 95% confidence interval, estimated using the Brookmeyer-Crowley method. CPS was defined as the ratio of the combined number of PD-L1 expressing tumor cells and immune cells (lymphocytes and macrophages) to the total number of viable tumor cells. Data for participants with a best overall response of CR or PR in the mITT population with PD-L1 CPS ≥1 are presented. 99999 = The median was not reached at the time of primary completion date, the lower and upper limit of the 95% CI was not calculable from the available data at the time of data cut off.

End point type	Secondary

End point timeframe:

Up to approximately 16 months

End point values	Feladilimab +pembrolizumab mITT analysis set	Placebo + pembrolizumab mITT analysis set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	31	39		
Units: Weeks				
median (confidence interval 95%)	99999 (99999	99999 (20.6 to		

to 99999)	99999)

Statistical analyses

No statistical analyses for this end point

Secondary: DoR per RECIST v1.1 in the PD-L1 CPS ≥20 population

End point title	DoR per RECIST v1.1 in the PD-L1 CPS ≥20 population

End point description:

DoR per RECIST v1.1 is defined as the time from first documented evidence of CR or PR until first documented disease progression per RECIST v1.1 based upon investigator assessment or death due to any cause, whichever occurs first, among participants who demonstrated CR or PR as the best overall response per RECIST v1.1. Kaplan-Meier estimate for the median DoR is presented, along with associated 95% confidence interval, estimated using the Brookmeyer-Crowley method. CPS was defined as the ratio of the combined number of PD-L1 expressing tumor cells and immune cells (lymphocytes and macrophages) to the total number of viable tumor cells. Data for participants with a best overall response of CR or PR in the mITT population with PD-L1 CPS ≥20 are presented. 99999 = The median was not reached at the time of primary completion date, the lower and upper limit of the 95% CI was not calculable from the available data at the time of data cut off.

End point type	Secondary

End point timeframe:

Up to approximately 16 months

End point values	Feladilimab +pembrolizumab mITT analysis set	Placebo + pembrolizumab mITT analysis set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	14	23		
Units: Weeks				
median (confidence interval 95%)	99999 (18.1 to 99999)	99999 (12.1 to 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: DCR per RECIST v1.1 in the PD-L1 CPS ≥20 population

End point title	DCR per RECIST v1.1 in the PD-L1 CPS ≥20 population

End point description:

DCR per RECIST v1.1 based upon investigator assessment, was defined as the percentage of participants with a best overall response of CR or PR at any time plus stable disease (SD) meeting the minimum time of 15 weeks. A status of SD≥15 weeks will be assigned if the follow-up disease assessment has met the SD criteria at least once after the date of randomization at a minimum of 14 weeks (98 days) considering a one-week visit window. Rate and associated 2-sided 95 percent Exact (Clopper-Pearson) Confidence Intervals are provided for each treatment arm which are unadjusted. CPS was defined as the ratio of the combined number of PD-L1 expressing tumor cells and immune cells

(lymphocytes and macrophages) to the total number of viable tumor cells. Data for participants who had a PD-L1 CPS of ≥20 are presented here.

End point type	Secondary

End point timeframe:

Up to approximately 16 months

End point values	Feladilimab +pembrolizumab mITT analysis set	Placebo + pembrolizumab mITT analysis set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	70	69		
Units: Percentage of Participants				
number (confidence interval 95%)	37.1 (25.9 to 49.5)	55.1 (42.6 to 67.1)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

The comparison between treatment groups was based on the stratified Miettinen & Nurminen method with strata weighting by sample size and a single treatment covariate. Stratification factors included HPV status (positive vs. negative). Participants with oropharynx HPV negative/unknown and non-oropharyngeal tumors were combined as the HPV negative group.

Comparison groups	Feladilimab +pembrolizumab mITT analysis set v Placebo + pembrolizumab mITT analysis set
Number of subjects included in analysis	139
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in Percentage
Point estimate	-18
Confidence interval	
level	95 %
sides	2-sided
lower limit	-33.7
upper limit	-1.4

Secondary: Number of participants with SAE by Severity

End point title	Number of participants with SAE by Severity

End point description:

A SAE was defined as any untoward medical occurrence that, at any dose results in death, is life-threatening, requires inpatient hospitalization or prolongation of existing hospitalization, results in persistent disability/incapacity, is a congenital anomaly/birth defect, any other situation such as important medical events according to medical or scientific judgement. Severity of each SAE was reported during the study and was assigned a grade according to the NCI-CTCAE. SAEs severity were graded on a 5-point scale as: 1 = mild; discomfort noticed, but no disruption to daily activity, 2 = moderate; discomfort sufficient to reduce or affect normal daily activity, 3 = severe; inability to work or perform normal daily activity, 4 = life-threatening consequences and 5 = death related to AE. Data of participants experiencing SAEs of Grade ≥3 have been presented.

End point type	Secondary
End point timeframe:	
Up to approximately 43 months	

End point values	Feladilimab + pembrolizumab safety analysis set	Placebo + pembrolizumab safety analysis set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	159	156		
Units: Participants				
Grade ≥3	43	46		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with AEs by severity

End point title	Number of participants with AEs by severity

End point description:

An AE was defined as any untoward medical occurrence in a clinical study participant, temporally associated with the use of a study intervention, whether or not considered related to the study intervention. Severity of each AE was reported during the study and was assigned a grade according to the National Cancer Institute- Common Toxicity Criteria for Adverse Events (NCI-CTCAE). AEs severity were graded on a 5-point scale as: 1 = mild; discomfort noticed, but no disruption to daily activity, 2 = moderate; discomfort sufficient to reduce or affect normal daily activity, 3 = severe; inability to work or perform normal daily activity, 4 = life-threatening consequences and 5 = death related to AE.

End point type	Secondary
End point timeframe:	
Up to approximately 43 months	

End point values	Feladilimab + pembrolizumab safety analysis set	Placebo + pembrolizumab safety analysis set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	159	156		
Units: Participants				
Grade 1	34	21		
Grade 2	48	54		
Grade 3	46	46		
Grade 4	7	6		
Grade 5	15	18		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with dose modifications

End point title	Number of participants with dose modifications

End point description:

Number of participants with dose modifications (including dose interruptions, dose delays and treatment discontinuations) were reported by each interventional component. 99999= The number of participants with treatment discontinuation by component did not receive the mentioned study intervention

End point type	Secondary

End point timeframe:

Up to approximately 16 months

End point values	Feladilimab + pembrolizumab safety analysis set	Placebo + pembrolizumab safety analysis set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	159	156		
Units: Participants				
Dose Interruption by component-feladilimab	4	99999		
Dose Interruption by component-placebo	99999	1		
Dose Interruption by component-pembrolizumab	0	1		
Dose delays by component- feladilimab	9	99999		
Dose delays by component- placebo	99999	5		
Dose delays by component-pembrolizumab	11	6		
Treatment discontinuation-feladilimab/placebo	159	154		
Treatment discontinuation-pembrolizumab	108	93		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with adverse events of special interest (AESI)

End point title	Number of participants with adverse events of special interest (AESI)

End point description:

AESI were defined as events of potential immunologic etiology, including immune-related AEs (irAEs). Such events recently reported after treatment with other immune modulatory therapy include colitis, uveitis, hepatitis, pneumonitis, diarrhea, endocrine disorders, and specific cutaneous toxicities, as well as other events that may be immune mediated.

End point type	Secondary

End point timeframe:

Up to approximately 43 months

End point values	Feladilimab + pembrolizumab safety analysis set	Placebo + pembrolizumab safety analysis set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	159	156		
Units: Participants	49	67		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with AESI by severity

End point title	Number of participants with AESI by severity

End point description:

AESI were defined as events of potential immunologic etiology, including immune-related AEs (irAEs). Such events recently reported after treatment with other immune modulatory therapy include colitis, uveitis, hepatitis, pneumonitis, diarrhea, endocrine disorders, and specific cutaneous toxicities, as well as other events that may be immune mediated. Severity of each AESI was reported during the study and was assigned a grade according to the NCI-CTCAE. AESIs severity were graded on a 5-point scale as: 1 = mild; discomfort noticed, but no disruption to daily activity, 2 = moderate; discomfort sufficient to reduce or affect normal daily activity, 3 = severe; inability to work or perform normal daily activity, 4 = life-threatening consequences and 5 = death related to AE. Data of participants experiencing AESIs of Grade ≥3 have been presented.

End point type	Secondary

End point timeframe:

Up to approximately 43 months

End point values	Feladilimab + pembrolizumab safety analysis set	Placebo + pembrolizumab safety analysis set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	159	156		
Units: Participants				
Grade >= 3	2	6		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to deterioration (TTD) in pain in the PD-L1 CPS ≥1 population

End point title	Time to deterioration (TTD) in pain in the PD-L1 CPS ≥1 population

End point description:

TTD in pain is defined as the time from randomization to the first definitive meaningful deterioration from baseline in the European Organization for Research and Treatment of Cancer Item Library(EORTC IL51) pain domain, i.e. an increase from baseline of at least 8.33 observed at all subsequent non-missing visits. The EORTC Quality of Life Questionnaire 35-Item Head and Neck Module (QLQ-H&N35) is a head and neck specific module with multi-item scales. The questionnaire scores for each scale and single-item measure are averaged and transformed linearly to present a score ranging from 0–100. A high score represents a high/healthy level of functioning. Data for participants in the mITT population with CPS ≥1 are presented here. 99999 = The upper limit of the 95% CI was not calculable from the available data at the time of data cut off.

End point type	Secondary

End point timeframe:

Up to approximately 16 months

End point values	Feladilimab +pembrolizumab mITT analysis set	Placebo + pembrolizumab mITT analysis set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	157	156		
Units: Months				
median (confidence interval 95%)	6.3 (5.1 to 99999)	10.4 (6.3 to 99999)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

The hazard ratio and 2-sided 95% CI was calculated from the Cox regression model with Efron's method of tie handling, a treatment covariate and stratified by PD-L1 expression (CPS ≥20 vs. 1≤ CPS <20) and HPV status (oropharynx HPV positive vs oropharynx HPV negative/unknown and non-oropharynx).

Comparison groups	Feladilimab +pembrolizumab mITT analysis set v Placebo + pembrolizumab mITT analysis set
Number of subjects included in analysis	313
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.783 [9]
Method	Stratified Cox proportional hazard model
Parameter estimate	Hazard ratio (HR)
Point estimate	1.17
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.78
upper limit	1.77

Notes:

[9] - Nominal p-value was calculated based on the one-sided log-rank test, stratified by PD-L1 expression (CPS ≥20 vs. 1≤ CPS <20) and HPV status (oropharynx HPV positive vs oropharynx HPV negative/unknown and non-oropharynx).

Secondary: TTD in pain in the PD-L1 CPS ≥20 population

End point title	TTD in pain in the PD-L1 CPS ≥20 population

End point description:

TTD in pain is defined as the time from randomization to the first definitive meaningful deterioration from baseline in the European Organization for Research and Treatment of Cancer Item Library(EORTC IL51) pain domain, i.e. an increase from baseline of at least 8.33 observed at all subsequent non-missing visits. The EORTC Quality of Life Questionnaire 35-Item Head and Neck Module (QLQ-H&N35) is a head and neck specific module with multi-item scales. The questionnaire scores for each scale and single-item measure are averaged and transformed linearly to present a score ranging from 0–100. A high score represents a high/healthy level of functioning. Data for participants who had a PD-L1 CPS of ≥20 are presented here. 99999 = The median was not reached at the time of primary completion date and the upper limit of the 95% CI was not calculable from the available data at the time of data cut off.

End point type	Secondary

End point timeframe:

Up to approximately 16 months

End point values	Feladilimab +pembrolizumab mITT analysis set	Placebo + pembrolizumab mITT analysis set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	70	69		
Units: Months				
median (confidence interval 95%)	99999 (5.1 to 99999)	12.0 (6.3 to 99999)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

The hazard ratio and 2-sided 95% CI was calculated from the Cox regression model with Efron's method of tie handling, a treatment covariate and stratified by HPV status (oropharynx HPV positive vs oropharynx HPV negative/unknown and non-oropharynx).

Comparison groups	Feladilimab +pembrolizumab mITT analysis set v Placebo + pembrolizumab mITT analysis set
Number of subjects included in analysis	139
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.5 [10]
Method	Stratified Cox proportional hazard model
Parameter estimate	Hazard ratio (HR)
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.5
upper limit	2

Notes:

[10] - Nominal p-value was calculated based on the one-sided log-rank test, stratified by HPV status (oropharynx HPV positive vs oropharynx HPV negative/unknown and non-oropharynx).

Secondary: TTD in physical function in the PD-L1 CPS ≥1 population

End point title	TTD in physical function in the PD-L1 CPS ≥1 population

End point description:

TTD in physical function is defined as the time from randomization to the first definitive meaningful deterioration from baseline in the PF T-score, i.e. a decrease from baseline of at least 2.4 observed at all subsequent non-missing visits, as measured by the PROMIS PF 8c. The PROMIS PF 8c is an 8-item fixed length short form derived from the PROMIS Physical Function item bank. It includes a 5-point scale with three sets of response options. Scores on the PROMIS PF 8c are reported on a T score metric (mean = 50 and SD = 10), with higher scores reflecting better physical functioning. Data for participants in the mITT population with CPS ≥1 are presented here.

End point type	Secondary

End point timeframe:

Up to approximately 16 months

End point values	Feladilimab +pembrolizumab mITT analysis set	Placebo + pembrolizumab mITT analysis set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	157	156		
Units: Months				
median (confidence interval 95%)	4.9 (3.5 to 7.7)	4.9 (3.0 to 6.3)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

The hazard ratio and 2-sided 95% CI was calculated from the Cox regression model with Efron's method of tie handling, a treatment covariate and stratified by PD-L1 expression (CPS ≥20 vs. 1≤ CPS <20) and HPV status (oropharynx HPV positive vs oropharynx HPV negative/unknown and non-oropharynx).

Comparison groups	Feladilimab +pembrolizumab mITT analysis set v Placebo + pembrolizumab mITT analysis set
Number of subjects included in analysis	313
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.329 [11]
Method	Stratified Cox proportional hazard model
Parameter estimate	Hazard ratio (HR)
Point estimate	0.91
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.62
upper limit	1.34

Notes:

[11] - Nominal p-value was calculated based on the one-sided log-rank test, stratified by PD-L1 expression (CPS ≥20 vs. 1≤ CPS <20) and HPV status (oropharynx HPV positive vs oropharynx HPV negative/unknown and non-oropharynx).

Secondary: TTD in physical function in the PD-L1 CPS ≥20 population

End point title	TTD in physical function in the PD-L1 CPS ≥20 population

End point description:

TTD in physical function is defined as the time from randomization to the first definitive meaningful

deterioration from baseline in the PF T-score, i.e. a decrease from baseline of at least 2.4 observed at all subsequent non-missing visits, as measured by the PROMIS PF 8c. The PROMIS PF 8c is an 8-item fixed length short form derived from the PROMIS Physical Function item bank. It includes a 5-point scale with three sets of response options. Scores on the PROMIS PF 8c are reported on a T score metric (mean = 50 and SD = 10), with higher scores reflecting better physical functioning. Data for participants who had a PD-L1 CPS of ≥20 are presented here. 99999 = The upper limit of the 95% CI was not calculable from the available data at the time of data cut off.

End point type	Secondary

End point timeframe:

Up to approximately 16 months

End point values	Feladilimab +pembrolizumab mITT analysis set	Placebo + pembrolizumab mITT analysis set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	70	69		
Units: Months				
median (confidence interval 95%)	4.9 (2.1 to 99999)	4.9 (3.1 to 99999)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

The hazard ratio and 2-sided 95% CI was calculated from the cox regression model with Efron's method of tie handling, a treatment covariate and stratified by HPV status (oropharynx HPV positive vs oropharynx HPV negative/unknown and non-oropharynx).

Comparison groups	Feladilimab +pembrolizumab mITT analysis set v Placebo + pembrolizumab mITT analysis set
Number of subjects included in analysis	139
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.608 [12]
Method	Stratified Cox proportional hazard model
Parameter estimate	Hazard ratio (HR)
Point estimate	1.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.6
upper limit	2

Notes:

[12] - Nominal p-value was calculated based on the one-sided log-rank test, stratified by HPV status (oropharynx HPV positive vs oropharynx HPV negative/unknown and non-oropharynx)

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All cause mortality, non-SAEs and SAEs were collected from Day 1 to Up to approximately 43 months.

Adverse event reporting additional description:

2 participants randomized to placebo arm, were dosed with feladilimab and included in the feladilimab arm. 1 participant randomized to feladilimab arm, never received feladilimab/placebo, was included in the placebo arm of the safety population.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	26.0

Reporting groups

Reporting group title	Participants receiving placebo and pembrolizumab

Reporting group description:

Participants were administered placebo and pembrolizumab as an IV infusion Q3W.

Reporting group title	Participants receiving feladilimab and pembrolizumab

Reporting group description:

Participants were administered feladilimab and pembrolizumab as an IV infusion once every Q3W.

Serious adverse events	Participants receiving placebo and pembrolizumab	Participants receiving feladilimab and pembrolizumab	
Total subjects affected by serious adverse events			
subjects affected / exposed	53 / 156 (33.97%)	52 / 159 (32.70%)	
number of deaths (all causes)	97	116	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cancer pain			
subjects affected / exposed	0 / 156 (0.00%)	1 / 159 (0.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infected neoplasm			
subjects affected / exposed	0 / 156 (0.00%)	1 / 159 (0.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Tumour haemorrhage			
subjects affected / exposed	6 / 156 (3.85%)	4 / 159 (2.52%)	
occurrences causally related to treatment / all	0 / 6	0 / 4	
deaths causally related to treatment / all	0 / 3	0 / 3	

Hypopharyngeal cancer			
subjects affected / exposed	1 / 156 (0.64%)	0 / 159 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Aortic aneurysm			
subjects affected / exposed	0 / 156 (0.00%)	1 / 159 (0.63%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Circulatory collapse			
subjects affected / exposed	1 / 156 (0.64%)	0 / 159 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Distributive shock			
subjects affected / exposed	1 / 156 (0.64%)	0 / 159 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Embolism			
subjects affected / exposed	0 / 156 (0.00%)	1 / 159 (0.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertension			
subjects affected / exposed	1 / 156 (0.64%)	0 / 159 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Shock haemorrhagic			
subjects affected / exposed	1 / 156 (0.64%)	0 / 159 (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			
Systemic inflammatory response syndrome			

subjects affected / exposed	1 / 156 (0.64%)	0 / 159 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	0 / 156 (0.00%)	1 / 159 (0.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain			
subjects affected / exposed	0 / 156 (0.00%)	1 / 159 (0.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General physical health deterioration			
subjects affected / exposed	1 / 156 (0.64%)	3 / 159 (1.89%)	
occurrences causally related to treatment / all	1 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Asthenia			
subjects affected / exposed	2 / 156 (1.28%)	1 / 159 (0.63%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Laryngeal haemorrhage			
subjects affected / exposed	1 / 156 (0.64%)	0 / 159 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute respiratory failure			
subjects affected / exposed	0 / 156 (0.00%)	1 / 159 (0.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Asphyxia			
subjects affected / exposed	0 / 156 (0.00%)	1 / 159 (0.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Aspiration			

subjects affected / exposed	0 / 156 (0.00%)	3 / 159 (1.89%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 2	
Chronic obstructive pulmonary disease			
subjects affected / exposed	2 / 156 (1.28%)	1 / 159 (0.63%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			
subjects affected / exposed	3 / 156 (1.92%)	4 / 159 (2.52%)	
occurrences causally related to treatment / all	0 / 3	1 / 4	
deaths causally related to treatment / all	0 / 2	0 / 0	
Pleural effusion			
subjects affected / exposed	1 / 156 (0.64%)	0 / 159 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Organising pneumonia			
subjects affected / exposed	0 / 156 (0.00%)	1 / 159 (0.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung disorder			
subjects affected / exposed	1 / 156 (0.64%)	0 / 159 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pharyngeal stenosis			
subjects affected / exposed	1 / 156 (0.64%)	0 / 159 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laryngeal obstruction			
subjects affected / exposed	0 / 156 (0.00%)	1 / 159 (0.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonitis			

subjects affected / exposed	1 / 156 (0.64%)	1 / 159 (0.63%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	1 / 156 (0.64%)	2 / 159 (1.26%)	
occurrences causally related to treatment / all	0 / 1	1 / 2	
deaths causally related to treatment / all	0 / 1	1 / 2	
Stridor			
subjects affected / exposed	0 / 156 (0.00%)	1 / 159 (0.63%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Interstitial lung disease			
subjects affected / exposed	0 / 156 (0.00%)	1 / 159 (0.63%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Blood creatinine increased			
subjects affected / exposed	2 / 156 (1.28%)	0 / 159 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic enzyme increased			
subjects affected / exposed	1 / 156 (0.64%)	0 / 159 (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			
Ankle fracture			
subjects affected / exposed	1 / 156 (0.64%)	0 / 159 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fracture			
subjects affected / exposed	0 / 156 (0.00%)	1 / 159 (0.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Limb injury			
subjects affected / exposed	1 / 156 (0.64%)	0 / 159 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural haemorrhage			
subjects affected / exposed	1 / 156 (0.64%)	1 / 159 (0.63%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tracheal haemorrhage			
subjects affected / exposed	0 / 156 (0.00%)	1 / 159 (0.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tracheal obstruction			
subjects affected / exposed	0 / 156 (0.00%)	1 / 159 (0.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femoral neck fracture			
subjects affected / exposed	1 / 156 (0.64%)	0 / 159 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Cardio-respiratory arrest			
subjects affected / exposed	1 / 156 (0.64%)	1 / 159 (0.63%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Nervous system disorders			
Epilepsy			
subjects affected / exposed	0 / 156 (0.00%)	1 / 159 (0.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhagic stroke			
subjects affected / exposed	0 / 156 (0.00%)	1 / 159 (0.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	

Neuralgia			
subjects affected / exposed	1 / 156 (0.64%)	0 / 159 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seizure			
subjects affected / exposed	1 / 156 (0.64%)	0 / 159 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal cord compression			
subjects affected / exposed	0 / 156 (0.00%)	1 / 159 (0.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	1 / 156 (0.64%)	3 / 159 (1.89%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Headache			
subjects affected / exposed	1 / 156 (0.64%)	0 / 159 (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			
Leukocytosis			
subjects affected / exposed	0 / 156 (0.00%)	1 / 159 (0.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anaemia			
subjects affected / exposed	1 / 156 (0.64%)	1 / 159 (0.63%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	0 / 156 (0.00%)	2 / 159 (1.26%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

Mouth haemorrhage			
subjects affected / exposed	2 / 156 (1.28%)	0 / 159 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Dysphagia			
subjects affected / exposed	4 / 156 (2.56%)	2 / 159 (1.26%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	2 / 156 (1.28%)	0 / 159 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Constipation			
subjects affected / exposed	1 / 156 (0.64%)	0 / 159 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oral cavity fistula			
subjects affected / exposed	2 / 156 (1.28%)	0 / 159 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oral pain			
subjects affected / exposed	0 / 156 (0.00%)	1 / 159 (0.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis			
subjects affected / exposed	0 / 156 (0.00%)	1 / 159 (0.63%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	1 / 156 (0.64%)	1 / 159 (0.63%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stomatitis			

subjects affected / exposed	1 / 156 (0.64%)	0 / 159 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal perforation			
subjects affected / exposed	0 / 156 (0.00%)	1 / 159 (0.63%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Pneumoperitoneum			
subjects affected / exposed	1 / 156 (0.64%)	0 / 159 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestinal obstruction			
subjects affected / exposed	1 / 156 (0.64%)	0 / 159 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pancreatitis acute			
subjects affected / exposed	0 / 156 (0.00%)	1 / 159 (0.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric ulcer			
subjects affected / exposed	1 / 156 (0.64%)	0 / 159 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Hepatotoxicity			
subjects affected / exposed	1 / 156 (0.64%)	0 / 159 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis			
subjects affected / exposed	2 / 156 (1.28%)	0 / 159 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			

Acute kidney injury			
subjects affected / exposed	1 / 156 (0.64%)	0 / 159 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematuria			
subjects affected / exposed	1 / 156 (0.64%)	0 / 159 (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			
Fistula discharge			
subjects affected / exposed	1 / 156 (0.64%)	0 / 159 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscular weakness			
subjects affected / exposed	1 / 156 (0.64%)	0 / 159 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Synovitis			
subjects affected / exposed	1 / 156 (0.64%)	0 / 159 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain in jaw			
subjects affected / exposed	1 / 156 (0.64%)	0 / 159 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Polyarthritis			
subjects affected / exposed	0 / 156 (0.00%)	1 / 159 (0.63%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Back pain			
subjects affected / exposed	0 / 156 (0.00%)	2 / 159 (1.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

Infections and infestations			
Abscess			
subjects affected / exposed	1 / 156 (0.64%)	0 / 159 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis			
subjects affected / exposed	0 / 156 (0.00%)	1 / 159 (0.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacteraemia			
subjects affected / exposed	0 / 156 (0.00%)	1 / 159 (0.63%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19			
subjects affected / exposed	4 / 156 (2.56%)	2 / 159 (1.26%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 2	0 / 1	
COVID-19 pneumonia			
subjects affected / exposed	2 / 156 (1.28%)	1 / 159 (0.63%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 2	0 / 0	
Cellulitis			
subjects affected / exposed	0 / 156 (0.00%)	1 / 159 (0.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infected skin ulcer			
subjects affected / exposed	0 / 156 (0.00%)	1 / 159 (0.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Localised infection			
subjects affected / exposed	0 / 156 (0.00%)	1 / 159 (0.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			

subjects affected / exposed	4 / 156 (2.56%)	4 / 159 (2.52%)	
occurrences causally related to treatment / all	0 / 4	2 / 6	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pulmonary sepsis			
subjects affected / exposed	1 / 156 (0.64%)	0 / 159 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Sepsis			
subjects affected / exposed	0 / 156 (0.00%)	2 / 159 (1.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin infection			
subjects affected / exposed	1 / 156 (0.64%)	1 / 159 (0.63%)	
occurrences causally related to treatment / all	1 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	0 / 156 (0.00%)	2 / 159 (1.26%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound infection			
subjects affected / exposed	0 / 156 (0.00%)	1 / 159 (0.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia aspiration			
subjects affected / exposed	4 / 156 (2.56%)	4 / 159 (2.52%)	
occurrences causally related to treatment / all	0 / 4	0 / 5	
deaths causally related to treatment / all	0 / 2	0 / 0	
Intervertebral discitis			
subjects affected / exposed	1 / 156 (0.64%)	0 / 159 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymph gland infection			

subjects affected / exposed	1 / 156 (0.64%)	0 / 159 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic shock			
subjects affected / exposed	1 / 156 (0.64%)	0 / 159 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Laryngitis			
subjects affected / exposed	0 / 156 (0.00%)	1 / 159 (0.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Cachexia			
subjects affected / exposed	1 / 156 (0.64%)	0 / 159 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypercalcaemia			
subjects affected / exposed	3 / 156 (1.92%)	2 / 159 (1.26%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoglycaemia			
subjects affected / exposed	0 / 156 (0.00%)	1 / 159 (0.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypokalaemia			
subjects affected / exposed	1 / 156 (0.64%)	2 / 159 (1.26%)	
occurrences causally related to treatment / all	1 / 1	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyponatraemia			
subjects affected / exposed	0 / 156 (0.00%)	1 / 159 (0.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malnutrition			

subjects affected / exposed	3 / 156 (1.92%)	0 / 159 (0.00%)	
occurrences causally related to treatment / all	1 / 3	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	Participants receiving placebo and pembrolizumab	Participants receiving feladilimab and pembrolizumab	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	128 / 156 (82.05%)	125 / 159 (78.62%)	
Investigations			
Weight decreased			
subjects affected / exposed	27 / 156 (17.31%)	20 / 159 (12.58%)	
occurrences (all)	29	20	
Blood alkaline phosphatase increased			
subjects affected / exposed	4 / 156 (2.56%)	8 / 159 (5.03%)	
occurrences (all)	4	9	
Aspartate aminotransferase increased			
subjects affected / exposed	11 / 156 (7.05%)	12 / 159 (7.55%)	
occurrences (all)	15	15	
Alanine aminotransferase increased			
subjects affected / exposed	12 / 156 (7.69%)	9 / 159 (5.66%)	
occurrences (all)	16	10	
Nervous system disorders			
Headache			
subjects affected / exposed	14 / 156 (8.97%)	15 / 159 (9.43%)	
occurrences (all)	17	19	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	21 / 156 (13.46%)	26 / 159 (16.35%)	
occurrences (all)	26	42	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	11 / 156 (7.05%)	11 / 159 (6.92%)	
occurrences (all)	12	13	
Fatigue			

subjects affected / exposed	29 / 156 (18.59%)	29 / 159 (18.24%)	
occurrences (all)	32	30	
Asthenia			
subjects affected / exposed	14 / 156 (8.97%)	17 / 159 (10.69%)	
occurrences (all)	23	17	
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	8 / 156 (5.13%)	12 / 159 (7.55%)	
occurrences (all)	8	15	
Constipation			
subjects affected / exposed	24 / 156 (15.38%)	22 / 159 (13.84%)	
occurrences (all)	26	28	
Diarrhoea			
subjects affected / exposed	13 / 156 (8.33%)	21 / 159 (13.21%)	
occurrences (all)	19	25	
Dysphagia			
subjects affected / exposed	15 / 156 (9.62%)	17 / 159 (10.69%)	
occurrences (all)	15	17	
Nausea			
subjects affected / exposed	17 / 156 (10.90%)	17 / 159 (10.69%)	
occurrences (all)	20	21	
Abdominal pain			
subjects affected / exposed	9 / 156 (5.77%)	5 / 159 (3.14%)	
occurrences (all)	11	6	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	19 / 156 (12.18%)	17 / 159 (10.69%)	
occurrences (all)	19	19	
Cough			
subjects affected / exposed	11 / 156 (7.05%)	11 / 159 (6.92%)	
occurrences (all)	11	14	
Productive cough			
subjects affected / exposed	8 / 156 (5.13%)	4 / 159 (2.52%)	
occurrences (all)	9	4	
Skin and subcutaneous tissue disorders			

Pruritus			
subjects affected / exposed	17 / 156 (10.90%)	11 / 159 (6.92%)	
occurrences (all)	19	15	
Rash			
subjects affected / exposed	21 / 156 (13.46%)	9 / 159 (5.66%)	
occurrences (all)	32	12	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	5 / 156 (3.21%)	15 / 159 (9.43%)	
occurrences (all)	5	15	
Anxiety			
subjects affected / exposed	3 / 156 (1.92%)	8 / 159 (5.03%)	
occurrences (all)	3	8	
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	16 / 156 (10.26%)	20 / 159 (12.58%)	
occurrences (all)	16	20	
Musculoskeletal and connective tissue disorders			
Neck pain			
subjects affected / exposed	12 / 156 (7.69%)	8 / 159 (5.03%)	
occurrences (all)	12	8	
Arthralgia			
subjects affected / exposed	11 / 156 (7.05%)	13 / 159 (8.18%)	
occurrences (all)	15	16	
Back pain			
subjects affected / exposed	10 / 156 (6.41%)	8 / 159 (5.03%)	
occurrences (all)	10	8	
Infections and infestations			
COVID-19			
subjects affected / exposed	9 / 156 (5.77%)	5 / 159 (3.14%)	
occurrences (all)	9	5	
Metabolism and nutrition disorders			
Hyponatraemia			
subjects affected / exposed	7 / 156 (4.49%)	13 / 159 (8.18%)	
occurrences (all)	7	25	
Hypokalaemia			

subjects affected / exposed	7 / 156 (4.49%)	11 / 159 (6.92%)	
occurrences (all)	10	17	
Hypercalcaemia			
subjects affected / exposed	8 / 156 (5.13%)	11 / 159 (6.92%)	
occurrences (all)	10	14	
Decreased appetite			
subjects affected / exposed	28 / 156 (17.95%)	15 / 159 (9.43%)	
occurrences (all)	28	15	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
24 October 2019	Amendment 1: Generated to provide additional clarification that PD-L1 immunohistochemistry (IHC) 22C3 pharmDx assay used by the central laboratories in determining PD-L1 CPS status for study eligibility was the US FDA approved and European Union (EU) CE marked PD-L1 IHC 22C3 pharmDx assay.
19 May 2020	Amendment 2: Generated to include eligibility criteria to restrict the population to have recurrence >6 months from completion of chemoradiation therapy, to address complications of rapid disease progression such as increased risk of tumor associated bleeding that was inherent to the underlying disease of HNSCC and additional clarification regarding unstable medical condition. Additional updates included accounting for the possibility of a non-proportional hazard effect and tail effect in the statistical plan; definition of second course of study treatment that was expanded to include participants who complete 35 cycles of study treatment.
29 June 2021	Amendment 3: Generated to update the Schedule of Activities (SoA), due to the study status in which there is no further accrual and feladilimab is no longer being administered

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported