



## 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:

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### 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                                                  |
| <b>Arm title</b>             | 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.

|                  |                                                  |
|------------------|--------------------------------------------------|
| <b>Arm title</b> | 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.

| <b>Number of subjects in period 1</b> | 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] $\geq 1$ ) population

|                 |                                                                                                             |
|-----------------|-------------------------------------------------------------------------------------------------------------|
| End point title | Overall survival (OS) in the PD-L1 expression positive (Combined positive score [CPS] $\geq 1$ ) 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  $\geq 1$  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 $\geq 20$ vs. $1 \leq \text{CPS} < 20$ ) 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 <sup>[1]</sup>                                                                   |
| 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  $\geq 20$  vs.  $1 \leq \text{CPS} < 20$ ) and HPV status (oropharynx HPV positive vs oropharynx HPV negative/unknown and non-oropharynx)

## Primary: OS in the PD-L1 expression high (CPS $\geq 20$ ) population

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                                             |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------|
| End point title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | OS in the PD-L1 expression high (CPS $\geq 20$ ) 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 $\geq 20$ 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:<br>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 $\geq 20$ vs. $1 \leq \text{CPS} < 20$ ) 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 <sup>[3]</sup>                                                                   |
| 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  $\geq 20$  vs.  $1 \leq \text{CPS} < 20$ ) 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 $\geq 1$ population

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |                                                                            |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------|
| End point title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | PFS per immune-based RECIST (iRECIST) in the PD-L1 CPS $\geq 1$ population |
| End point description:<br>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 $\geq 1$ 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  $\geq 20$  vs.  $1 \leq \text{CPS} < 20$ ) 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 <sup>[4]</sup>                                                                   |
| 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  $\geq 20$  vs.  $1 \leq \text{CPS} < 20$ ) and HPV status (oropharynx HPV positive vs oropharynx HPV negative/unknown and non-oropharynx).

## Secondary: PFS per RECIST in the PD-L1 CPS $\geq 20$ population

|                 |                                                      |
|-----------------|------------------------------------------------------|
| End point title | PFS per RECIST in the PD-L1 CPS $\geq 20$ 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  $\geq 20$  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

| <b>End point values</b>          | 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

| <b>Statistical analysis title</b>                                                                                                                                                                                                                        | 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                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                        |

| <b>End point values</b>          | 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

| <b>Statistical analysis title</b>                                                                                                                                                                                                                                                              | Statistical Analysis 1                                                                   |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------|
| Statistical analysis description:<br>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:<br>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 24 months in the PD-L1 CPS $\geq 1$ population

|                                                                                                                                                                                                                                                           |                                                                     |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------|
| End point title                                                                                                                                                                                                                                           | Milestone OS rate at 24 months in the PD-L1 CPS $\geq 1$ population |
| End point description:<br>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:<br>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 <sup>[5]</sup>                             | 0 <sup>[6]</sup>                          |  |  |
| 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 12 months in the PD-L1 CPS $\geq 20$ population

|                                                                                                                                                                                                                                                                                                                                                                                                                                             |                                                                      |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------|
| End point title                                                                                                                                                                                                                                                                                                                                                                                                                             | Milestone OS rate at 12 months in the PD-L1 CPS $\geq 20$ population |
| End point description:<br>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 $\geq 20$ 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 $\geq 20$ population

|                 |                                                                      |
|-----------------|----------------------------------------------------------------------|
| End point title | Milestone OS rate at 24 months in the PD-L1 CPS $\geq 20$ 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 <sup>[7]</sup>                             | 0 <sup>[8]</sup>                          |  |  |
| 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: ORR per RECIST v1.1 in the PD-L1 CPS $\geq 20$ population

|                 |                                                           |
|-----------------|-----------------------------------------------------------|
| End point title | ORR per RECIST v1.1 in the PD-L1 CPS $\geq 20$ 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  $\geq 20$  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**

|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | 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  $\geq 1$  population**

|                 |                                                          |
|-----------------|----------------------------------------------------------|
| End point title | ORR per RECIST v1.1 in the PD-L1 CPS $\geq 1$ 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  $\geq 1$  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  $\geq 20$  vs.  $1 \leq$  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: DCR per RECIST v1.1 in the PD-L1 CPS $\geq 1$ population

|                 |                                                          |
|-----------------|----------------------------------------------------------|
| End point title | DCR per RECIST v1.1 in the PD-L1 CPS $\geq 1$ 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  $\geq 15$  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  $\geq 1$  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  $\geq 20$  vs.  $1 \leq \text{CPS} < 20$ ) 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: DCR per RECIST v1.1 in the PD-L1 CPS $\geq 20$ population

|                 |                                                           |
|-----------------|-----------------------------------------------------------|
| End point title | DCR per RECIST v1.1 in the PD-L1 CPS $\geq 20$ 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 $\geq 15$  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  $\geq 20$  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

|                                   |                        |
|-----------------------------------|------------------------|
| <b>Statistical analysis title</b> | 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: Duration of response (DoR) per RECIST v1.1 in the PD-L1 CPS $\geq 1$ population

|                 |                                                                                 |
|-----------------|---------------------------------------------------------------------------------|
| End point title | Duration of response (DoR) per RECIST v1.1 in the PD-L1 CPS $\geq 1$ 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  $\geq 1$  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 to 99999)                       | 99999 (20.6 to 99999)                     |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: DoR per RECIST v1.1 in the PD-L1 CPS $\geq 20$ population

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                                           |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------|
| End point title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | DoR per RECIST v1.1 in the PD-L1 CPS $\geq 20$ 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 $\geq 20$ 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: 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: 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 SAE by Severity

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |                                             |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------|
| End point title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | Number of participants with SAE by Severity |
| End point description:<br>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 $\geq 3$ have been presented. |                                             |
| End point type                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | Secondary                                   |
| End point timeframe:<br>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 $\geq 3$              | 43                                              | 46                                          |  |  |

## 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 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 AESI by severity

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                              |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------|
| End point title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | Number of participants with AESI by severity |
| End point description:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                                              |
| <p>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 <math>\geq 3</math> have been presented.</p> |                                              |
| 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 $\geq 3$              | 2                                               | 6                                           |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Time to deterioration (TTD) in pain in the PD-L1 CPS $\geq 1$ population

|                 |                                                                          |
|-----------------|--------------------------------------------------------------------------|
| End point title | Time to deterioration (TTD) in pain in the PD-L1 CPS $\geq 1$ 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  $\geq 1$  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  $\geq 20$  vs.  $1 \leq \text{CPS} < 20$ ) 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 <sup>[9]</sup>                                                                    |
| 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  $\geq 20$  vs.  $1 \leq \text{CPS} < 20$ ) and HPV status (oropharynx HPV positive vs oropharynx HPV negative/unknown and non-oropharynx).

## Secondary: TTD in pain in the PD-L1 CPS $\geq 20$ population

|                 |                                                   |
|-----------------|---------------------------------------------------|
| End point title | TTD in pain in the PD-L1 CPS $\geq 20$ 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  $\geq 20$  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 <sup>[10]</sup>                                                                    |
| 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 $\geq 1$ population

|                 |                                                               |
|-----------------|---------------------------------------------------------------|
| End point title | TTD in physical function in the PD-L1 CPS $\geq 1$ 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  $\geq 1$  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  $\geq 20$  vs.  $1 \leq \text{CPS} < 20$ ) 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 <sup>[11]</sup>                                                                   |
| 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  $\geq 20$  vs.  $1 \leq \text{CPS} < 20$ ) and HPV status (oropharynx HPV positive vs oropharynx HPV negative/unknown and non-oropharynx).

**Secondary: TTD in physical function in the PD-L1 CPS  $\geq 20$  population**

|                 |                                                                |
|-----------------|----------------------------------------------------------------|
| End point title | TTD in physical function in the PD-L1 CPS $\geq 20$ 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  $\geq 20$  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 <sup>[12]</sup>                                                                  |
| 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.

| <b>Serious adverse events</b>                                       | 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<br>Abscess<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all | 1 / 156 (0.64%)<br>0 / 1<br>0 / 0 | 0 / 159 (0.00%)<br>0 / 0<br>0 / 0 |  |
| Appendicitis<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all                           | 0 / 156 (0.00%)<br>0 / 0<br>0 / 0 | 1 / 159 (0.63%)<br>0 / 1<br>0 / 0 |  |
| Bacteraemia<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all                            | 0 / 156 (0.00%)<br>0 / 0<br>0 / 0 | 1 / 159 (0.63%)<br>1 / 1<br>0 / 0 |  |
| COVID-19<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all                               | 4 / 156 (2.56%)<br>0 / 4<br>0 / 2 | 2 / 159 (1.26%)<br>0 / 2<br>0 / 1 |  |
| COVID-19 pneumonia<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all                     | 2 / 156 (1.28%)<br>0 / 2<br>0 / 2 | 1 / 159 (0.63%)<br>0 / 1<br>0 / 0 |  |
| Cellulitis<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all                             | 0 / 156 (0.00%)<br>0 / 0<br>0 / 0 | 1 / 159 (0.63%)<br>0 / 1<br>0 / 0 |  |
| Infected skin ulcer<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all                    | 0 / 156 (0.00%)<br>0 / 0<br>0 / 0 | 1 / 159 (0.63%)<br>0 / 1<br>0 / 0 |  |
| Localised infection<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all                    | 0 / 156 (0.00%)<br>0 / 0<br>0 / 0 | 1 / 159 (0.63%)<br>0 / 1<br>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 %

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

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported