



## Clinical trial results:

### A Phase 2 Study of INCMGA00012 in Participants With Metastatic Merkel Cell Carcinoma

#### Summary

|                          |                         |
|--------------------------|-------------------------|
| EudraCT number           | 2018-001627-39          |
| Trial protocol           | CZ DE FR ES GB PL HU IT |
| Global end of trial date | 27 June 2024            |

#### Results information

|                                |  |
|--------------------------------|--|
| Result version number          | v2 (current)   |
| This version publication date  | 31 July 2025   |
| First version publication date | 26 June 2025   |
| Version creation reason        | <ul style="list-style-type: none"><li>• Correction of full data set</li></ul> Revised to align with changes made to ClinicalTrials.gov results record. |

#### Trial information

##### Trial identification

|                       |                 |
|-----------------------|-----------------|
| Sponsor protocol code | INCMGA 0012-201 |
|-----------------------|-----------------|

##### Additional study identifiers

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

Notes:

#### Sponsors

|                              |  |
|------------------------------|--|
| Sponsor organisation name    | Incyte Corporation   |
| Sponsor organisation address | 1801 Augustine Cutoff, Wilmington, United States, 19803              |
| Public contact               | Study Director, Incyte Corporation, 1 8554633463, medinfo@incyte.com |
| Scientific contact           | Study Director, Incyte Corporation, 1 8554633463, medinfo@incyte.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                       | 27 June 2024 |
| Is this the analysis of the primary completion data? | No           |

|                                  |              |
|----------------------------------|--------------|
| Global end of trial reached?     | Yes          |
| Global end of trial date         | 27 June 2024 |
| Was the trial ended prematurely? | No           |

Notes:

## General information about the trial

Main objective of the trial:

This study was conducted to determine the efficacy of retifanlimab in terms of the objective response rate in chemotherapy-naïve participants with metastatic Merkel Cell carcinoma (MCC).

Protection of trial subjects:

This study was performed in accordance with ethical principles that have their origin in the Declaration of Helsinki and was conducted in adherence to the study Protocol, applicable Good Clinical Practices, and applicable laws and country-specific regulations in which the study was conducted.

Background therapy: -

Evidence for comparator: -

|   |                  |
|---|------------------|
| Actual start date of recruitment                          | 25 February 2019 |
| Long term follow-up planned                               | No               |
| Independent data monitoring committee (IDMC) involvement? | No               |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |                   |
|--------------------------------------|-------------------|
| Country: Number of subjects enrolled | Canada: 7         |
| Country: Number of subjects enrolled | Switzerland: 3    |
| Country: Number of subjects enrolled | Czechia: 2        |
| Country: Number of subjects enrolled | Germany: 2        |
| Country: Number of subjects enrolled | Spain: 2          |
| Country: Number of subjects enrolled | France: 22        |
| Country: Number of subjects enrolled | United Kingdom: 1 |
| Country: Number of subjects enrolled | Hungary: 3        |
| Country: Number of subjects enrolled | Italy: 40         |
| Country: Number of subjects enrolled | Poland: 9         |
| Country: Number of subjects enrolled | United States: 16 |
| Worldwide total number of subjects   | 107               |
| EEA total number of subjects         | 80                |

Notes:

### Subjects enrolled per age group

|  |   |
|--|---|
| In utero                               | 0 |
| Preterm newborn - gestational age < 37 | 0 |

|  |    |
|--|----|
| wk                                       |    |
| Newborns (0-27 days)                     | 0  |
| Infants and toddlers (28 days-23 months) | 0  |
| Children (2-11 years)                    | 0  |
| Adolescents (12-17 years)                | 0  |
| Adults (18-64 years)                     | 35 |
| From 65 to 84 years                      | 63 |
| 85 years and over                        | 9  |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

Participants were enrolled and treated at 34 study centers in Italy, France, the United States, Poland, Canada, Switzerland, Hungary, the Czech Republic, Germany, Spain, and the United Kingdom.

### Period 1

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

### Arms

|                              |                     |
|------------------------------|---------------------|
| Are arms mutually exclusive? | Yes                 |
| <b>Arm title</b>             | Chemotherapy: Naïve |

Arm description:

Participants with recurrent, advanced locoregional disease or distant metastatic disease who did not receive any prior chemotherapy received retifanlimab 500 milligrams (mg), administered by intravenous (IV) infusion over 60 minutes on Day 1 of each 28-day cycle (Q4W).

|  |                       |
|--|-----------------------|
| Arm type                               | Experimental          |
| Investigational medicinal product name | retifanlimab          |
| Investigational medicinal product code |                       |
| Other name                             |                       |
| Pharmaceutical forms                   | Solution for infusion |
| Routes of administration               | Intravenous use       |

Dosage and administration details:

unit dose strength/dosage level = 500 mg Q4W; administered over 60 minutes (+ 15 minutes)

|                  |                          |
|------------------|--------------------------|
| <b>Arm title</b> | Chemotherapy: Refractory |
|------------------|--------------------------|

Arm description:

Participants with disease not responding to prior chemotherapy received retifanlimab 500 mg, administered by IV infusion over 60 minutes on Day 1 Q4W.

|  |                       |
|--|-----------------------|
| Arm type                               | Experimental          |
| Investigational medicinal product name | retifanlimab          |
| Investigational medicinal product code |                       |
| Other name                             |                       |
| Pharmaceutical forms                   | Solution for infusion |
| Routes of administration               | Intravenous use       |

Dosage and administration details:

unit dose strength/dosage level = 500 mg Q4W; administered over 60 minutes (+ 15 minutes)

| <b>Number of subjects in period 1</b> | <b>Chemotherapy:<br/>Naïve</b> | <b>Chemotherapy:<br/>Refractory</b> |
|---------------------------------------|--------------------------------|-------------------------------------|
| Started                               | 101                            | 6                                   |
| Safety Evaluable Population           | 101                            | 6                                   |
| Enrolled Population                   | 101                            | 6                                   |
| Full Analysis Set                     | 65                             | 6                                   |
| Completed                             | 0                              | 0                                   |
| Not completed                         | 101                            | 6                                   |
| Consent withdrawn by subject          | 17                             | -                                   |
| Death                                 | 38                             | 3                                   |
| Lost to follow-up                     | 4                              | -                                   |
| Discontinued Due to End of Study      | 42                             | 3                                   |

## Baseline characteristics

### Reporting groups

|   |                          |
|---|--------------------------|
| Reporting group title   | Chemotherapy: Naïve      |
| Reporting group description:  |                          |
| Participants with recurrent, advanced locoregional disease or distant metastatic disease who did not receive any prior chemotherapy received retifanlimab 500 milligrams (mg), administered by intravenous (IV) infusion over 60 minutes on Day 1 of each 28-day cycle (Q4W). |                          |
| Reporting group title   | Chemotherapy: Refractory |
| Reporting group description:  |                          |
| Participants with disease not responding to prior chemotherapy received retifanlimab 500 mg, administered by IV infusion over 60 minutes on Day 1 Q4W.  |                          |

| Reporting group values                             | Chemotherapy: Naïve | Chemotherapy: Refractory | Total |
|--|---------------------|--------------------------|-------|
| Number of subjects                                 | 101                 | 6                        | 107   |
| Age Categorical<br>Units: Subjects                 |                     |                          |       |
| In utero   | 0                   | 0                        | 0     |
| Preterm newborn infants (gestational age < 37 wks) | 0                   | 0                        | 0     |
| Newborns (0-27 days)                               | 0                   | 0                        | 0     |
| Infants and toddlers (28 days-23 months)           | 0                   | 0                        | 0     |
| Children (2-11 years)                              | 0                   | 0                        | 0     |
| Adolescents (12-17 years)                          | 0                   | 0                        | 0     |
| Adults (18-64 years)                               | 32                  | 3                        | 35    |
| From 65-84 years                                   | 60                  | 3                        | 63    |
| 85 years and over                                  | 9                   | 0                        | 9     |
| Age Continuous<br>Units: years                     |                     |                          |       |
| arithmetic mean                                    | 71.1                | 63.8                     |       |
| standard deviation                                 | ± 10.44             | ± 10.46                  | -     |
| Gender Categorical<br>Units: Subjects              |                     |                          |       |
| Female   | 33                  | 1                        | 34    |
| Male   | 68                  | 5                        | 73    |
| Race<br>Units: Subjects                            |                     |                          |       |
| Asian  | 1                   | 0                        | 1     |
| White  | 78                  | 6                        | 84    |
| Unknown or Not Reported                            | 22                  | 0                        | 22    |
| Ethnicity<br>Units: Subjects                       |                     |                          |       |
| Hispanic or Latino                                 | 1                   | 0                        | 1     |
| Not Hispanic or Latino                             | 75                  | 6                        | 81    |
| Unknown or Not Reported                            | 25                  | 0                        | 25    |

## End points

### End points reporting groups

|   |                                 |
|---|---------------------------------|
| Reporting group title   | Chemotherapy: Naïve             |
| Reporting group description:<br>Participants with recurrent, advanced locoregional disease or distant metastatic disease who did not receive any prior chemotherapy received retifanlimab 500 milligrams (mg), administered by intravenous (IV) infusion over 60 minutes on Day 1 of each 28-day cycle (Q4W). |                                 |
| Reporting group title   | Chemotherapy: Refractory        |
| Reporting group description:<br>Participants with disease not responding to prior chemotherapy received retifanlimab 500 mg, administered by IV infusion over 60 minutes on Day 1 Q4W.  |                                 |
| Subject analysis set title  | All Participants: PK Population |
| Subject analysis set type   | Full analysis                   |
| Subject analysis set description:<br>Participants with recurrent, advanced locoregional disease or distant metastatic disease who did not receive any prior chemotherapy received retifanlimab 500 mg, administered by IV infusion over 60 minutes on Day 1 Q4W.  |                                 |

### Primary: Objective Response Rate (ORR)

|   |  |
|---|--|
| End point title   | Objective Response Rate (ORR) <sup>[1]</sup> |
| End point description:<br>ORR=percentage of participants with a confirmed overall response of complete response (CR) or partial response (PR), per Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1 (v1.1), as determined by Independent Central Radiographic Review (ICR), at any post-Baseline visit until the first progressive disease (PD) or new anti-cancer therapy. CR: disappearance of all target/non-target lesions and no appearance of new lesions. Any pathological lymph nodes (target or non-target) must have a reduction in the short axis to <10 millimeters (mm). PR: complete disappearance or ≥30% decrease in the sum of the diameters of target lesions, taking as a reference the baseline sum diameters, no new lesions, and no progression of non-target lesions. Full Analysis Set (FAS): all enrolled participants who received ≥1 dose of study drug as of 15 October 2020 (selected to allow for ≥60 chemotherapy-naïve participants to be followed for at least 6 months after first response assessment). |  |
| End point type  | Primary                                      |
| End point timeframe:<br>up to 26.8 months   |  |

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Statistical analysis was not conducted for this endpoint.

| End point values                  | Chemotherapy: Naïve | Chemotherapy: Refractory |  |  |
|-----------------------------------|---------------------|--------------------------|--|--|
| Subject group type                | Reporting group     | Reporting group          |  |  |
| Number of subjects analysed       | 65 <sup>[2]</sup>   | 0 <sup>[3]</sup>         |  |  |
| Units: percentage of participants |                     |                          |  |  |
| number (confidence interval 95%)  | 52.3 (39.5 to 64.9) | ( to )                   |  |  |

Notes:

[2] - FAS. Analysis was based on the chemotherapy-naïve subset of the FAS.

[3] - FAS. Analysis was based on the chemotherapy-naïve subset of the FAS.

### Statistical analyses

No statistical analyses for this end point

**Secondary: Duration of response (DOR)**

|                 |                            |
|-----------------|----------------------------|
| End point title | Duration of response (DOR) |
|-----------------|----------------------------|

End point description:

DOR=time from an initial objective response (CR or PR) per RECIST v1.1 until PD, or death due to any cause, as determined by ICR. CR: disappearance of all target/non-target lesions and no appearance of any new lesions. Any pathological lymph nodes (target or non-target) must have a reduction in the short axis to <10 mm. PR: complete disappearance or a  $\geq 30\%$  decrease in the sum of the diameters of target lesions, taking as a reference the baseline sum diameters, no new lesions, and no progression of non-target lesions. PD: progression of a target or non-target lesion or presence of a new lesion. A Kaplan-Meier estimate (estimated median) of the distribution function is reported. Safety Evaluable Population (SAP): all enrolled participants who received  $\geq 1$  dose of study drug. Analysis was based on the chemotherapy-naïve subset of the population. 9999=The median and the upper limit of the confidence interval were not estimable because too few participants had disease progression or died.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

up to 55.3 months

| End point values                 | Chemotherapy: Naïve  | Chemotherapy: Refractory |  |  |
|----------------------------------|----------------------|--------------------------|--|--|
| Subject group type               | Reporting group      | Reporting group          |  |  |
| Number of subjects analysed      | 55 <sup>[4]</sup>    | 0 <sup>[5]</sup>         |  |  |
| Units: months                    |                      |                          |  |  |
| number (confidence interval 95%) | 9999 (22.87 to 9999) | ( to )                   |  |  |

Notes:

[4] - SAP. Participants with confirmed CR/PR prior to PD or start of new anticancer therapy were assessed.

[5] - SAP. Participants with confirmed CR/PR prior to PD or start of new anticancer therapy were assessed.

**Statistical analyses**

No statistical analyses for this end point

**Secondary: Number of participants with any treatment-emergent adverse event (TEAE)**

|                 |   |
|-----------------|---|
| End point title | Number of participants with any treatment-emergent adverse event (TEAE) |
|-----------------|---|

End point description:

An adverse event (AE) is any untoward medical occurrence associated with the use of a drug in humans, whether or not considered drug related. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease (new or exacerbated) temporally associated with the use of study treatment. A TEAE was defined as either an AE reported for the first time or a worsening of a pre-existing event after the first dose of study drug until 90 days after the last dose of study drug. An AE with onset on/after starting a new anticancer therapy was not summarized as a TEAE.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

up to 846 days (up to approximately 2.3 years)



| End point values            | Chemotherapy:<br>Naïve | Chemotherapy:<br>Refractory |  |  |
|-----------------------------|------------------------|-----------------------------|--|--|
| Subject group type          | Reporting group        | Reporting group             |  |  |
| Number of subjects analysed | 101 <sup>[6]</sup>     | 6 <sup>[7]</sup>            |  |  |
| Units: participants         |                        |                             |  |  |
| number (not applicable)     | 92                     | 5                           |  |  |

Notes:

[6] - Safety Evaluable Population

[7] - Safety Evaluable Population

## Statistical analyses

No statistical analyses for this end point

## Secondary: Overall Survival

|                 |                  |
|-----------------|------------------|
| End point title | Overall Survival |
|-----------------|------------------|

End point description:

Overall survival was defined as the time in months between the first dose date (Day 1) and the date of death due to any cause. Analysis was based on the chemotherapy-naïve subset of the population. Median overall survival time was estimated using the Kaplan-Meier method. CI for median overall survival time was calculated using the method of Brookmeyer and Crowley. 9999=The median and the upper limit of the confidence interval were not estimable because too few participants died.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

up to 60.4 months

| End point values                 | Chemotherapy:<br>Naïve | Chemotherapy:<br>Refractory |  |  |
|----------------------------------|------------------------|-----------------------------|--|--|
| Subject group type               | Reporting group        | Reporting group             |  |  |
| Number of subjects analysed      | 101 <sup>[8]</sup>     | 0 <sup>[9]</sup>            |  |  |
| Units: months                    |                        |                             |  |  |
| median (confidence interval 95%) | 9999 (45.24 to 9999)   | ( to )                      |  |  |

Notes:

[8] - Safety Evaluable Population

[9] - Safety Evaluable Population

## Statistical analyses

No statistical analyses for this end point

## Secondary: Disease Control Rate (DCR)

|                 |                            |
|-----------------|----------------------------|
| End point title | Disease Control Rate (DCR) |
|-----------------|----------------------------|

End point description:

DCR was defined as the percentage of participants with a confirmed overall response (CR and PR) or stable disease (SD) (non-CR/non-PD) lasting at least 6 months from the start of treatment, until the first PD or new anti-cancer therapy, per RECIST v1.1 as determined by ICR. CR: disappearance of all target and non-target lesions and no appearance of any new lesions. Any pathological lymph nodes (whether target or non-target) must have a reduction in the short axis to <10 mm. PR: complete disappearance or at least a 30% decrease in the sum of the diameters of target lesions, taking as a reference the baseline sum diameters, no new lesions, and no progression of non-target lesions. PD: progression of a target or non-target lesion or presence of a new lesion. SD: no change in target lesions to qualify for CR, PR, or PD. Analysis was based on the chemotherapy-naïve subset of the population. CIs were calculated based on the exact method for binomial distributions.

|   |           |
|---|-----------|
| End point type                            | Secondary |
| End point timeframe:<br>up to 57.1 months |           |

| End point values                  | Chemotherapy:<br>Naïve | Chemotherapy:<br>Refractory |  |  |
|-----------------------------------|------------------------|-----------------------------|--|--|
| Subject group type                | Reporting group        | Reporting group             |  |  |
| Number of subjects analysed       | 101 <sup>[10]</sup>    | 0 <sup>[11]</sup>           |  |  |
| Units: percentage of participants |                        |                             |  |  |
| number (confidence interval 95%)  | 60.4 (50.2 to 70.0)    | ( to )                      |  |  |

Notes:

[10] - Safety Evaluable Population

[11] - Safety Evaluable Population

## Statistical analyses

No statistical analyses for this end point

## Secondary: Progression-free Survival (PFS)

|   |                                 |
|---|---------------------------------|
| End point title   | Progression-free Survival (PFS) |
| End point description:  |                                 |
| According to RESIST v1.1, PFS was defined the time from the start of therapy until disease progression, or death due to any cause, as determined by ICR. Evaluation of target lesions: PD: ≥20% increase in the sum of diameters of target lesions, taking as reference the smallest sum on study. The sum must also demonstrate an absolute increase of at least 5 mm. (Note: the appearance of one or more new lesions is also considered PD). Evaluation of non-target lesions: PD: Unequivocal progression of existing non-target lesions. (Note: the appearance of one or more new lesions is also considered PD). Analysis was based on the chemotherapy-naïve subset of the population. Median PFS time was estimated using the Kaplan-Meier method. The CI for median PFS time was calculated using the method of Brookmeyer and Crowley. |                                 |
| End point type  | Secondary                       |
| End point timeframe:<br>up to 57.1 months   |                                 |

| End point values                 | Chemotherapy:<br>Naïve | Chemotherapy:<br>Refractory |  |  |
|----------------------------------|------------------------|-----------------------------|--|--|
| Subject group type               | Reporting group        | Reporting group             |  |  |
| Number of subjects analysed      | 101 <sup>[12]</sup>    | 0 <sup>[13]</sup>           |  |  |
| Units: months                    |                        |                             |  |  |
| median (confidence interval 95%) | 16.03 (9.03 to 32.23)  | ( to )                      |  |  |

Notes:

[12] - Safety Evaluable Population

[13] - Safety Evaluable Population

## Statistical analyses

No statistical analyses for this end point

**Secondary: First-dose Cmax of retifanlimab**

|                 |                                 |
|-----------------|---------------------------------|
| End point title | First-dose Cmax of retifanlimab |
|-----------------|---------------------------------|

End point description:

Cmax was defined as the maximum observed plasma concentration. The Pharmacokinetic (PK) Evaluable Population was comprised of all participants who received at least 1 dose of study drug and have provided a Baseline and at least 1 post-dose PK sample.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

preinfusion, 10 minutes postinfusion ( $\pm$  10 minutes), and 4 hours postinfusion ( $\pm$  10 minutes) on Day 1 of Cycle 1

| End point values                                      | All Participants: PK Population |  |  |  |
|---|---------------------------------|--|--|--|
| Subject group type                                    | Subject analysis set            |  |  |  |
| Number of subjects analysed                           | 102 <sup>[14]</sup>             |  |  |  |
| Units: micrograms per milliliter ( $\mu\text{g/mL}$ ) |                                 |  |  |  |
| arithmetic mean (standard deviation)                  | 144 ( $\pm$ 32.6)               |  |  |  |

Notes:

[14] - PK Evaluable Population

**Statistical analyses**

No statistical analyses for this end point

**Secondary: First-dose Cmin of retifanlimab**

|                 |                                 |
|-----------------|---------------------------------|
| End point title | First-dose Cmin of retifanlimab |
|-----------------|---------------------------------|

End point description:

Cmin was defined as the minimum observed plasma concentration over the dose interval.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

preinfusion, 10 minutes postinfusion ( $\pm$  10 minutes), and 4 hours postinfusion ( $\pm$  10 minutes) on Day 1 of Cycle 1

| End point values                     | All Participants: PK Population |  |  |  |
|--------------------------------------|---------------------------------|--|--|--|
| Subject group type                   | Subject analysis set            |  |  |  |
| Number of subjects analysed          | 102 <sup>[15]</sup>             |  |  |  |
| Units: $\mu\text{g/mL}$              |                                 |  |  |  |
| arithmetic mean (standard deviation) | 20.5 ( $\pm$ 7.23)              |  |  |  |

Notes:

[15] - PK Evaluable Population

**Statistical analyses**

No statistical analyses for this end point

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**Secondary: First-dose AUC0-t of retifanlimab**

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|                 |                                   |
|-----------------|-----------------------------------|
| End point title | First-dose AUC0-t of retifanlimab |
|-----------------|-----------------------------------|

End point description:

AUC0-t was defined as the area under the plasma concentration-time curve from time zero to time t.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

preinfusion, 10 minutes postinfusion ( $\pm$  10 minutes), and 4 hours postinfusion ( $\pm$  10 minutes) on Day 1 of Cycle 1

---

| End point values                     | All Participants: PK Population |  |  |  |
|--------------------------------------|---------------------------------|--|--|--|
| Subject group type                   | Subject analysis set            |  |  |  |
| Number of subjects analysed          | 102 <sup>[16]</sup>             |  |  |  |
| Units: day*mg/L                      |                                 |  |  |  |
| arithmetic mean (standard deviation) | 1770 ( $\pm$ 549)               |  |  |  |

Notes:

[16] - PK Evaluable Population

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**Statistical analyses**

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No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Deaths were assessed for up to 60.4 months. Adverse events were assessed for up to 846 days (up to approximately 2.3 years).

Adverse event reporting additional description:

TEAEs (AEs reported for the first time/worsening of pre-existing events after the first dose of study drug until 90 days after the last dose of study drug) are reported for the Safety Evaluable Population (enrolled participants who received  $\geq 1$  dose of study drug). AEs with onset on/after starting new anticancer therapy were not summarized as TEAEs.

|                 |            |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

### Dictionary used

|                 |        |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

|                    |      |
|--------------------|------|
| Dictionary version | 26.1 |
|--------------------|------|

### Reporting groups

|                       |                     |
|-----------------------|---------------------|
| Reporting group title | Chemotherapy: Naïve |
|-----------------------|---------------------|

Reporting group description:

Participants with recurrent, advanced locoregional disease or distant metastatic disease who did not receive any prior chemotherapy received retifanlimab 500 milligrams (mg), administered by intravenous (IV) infusion over 60 minutes on Day 1 of each 28-day cycle (Q4W).

|                       |                          |
|-----------------------|--------------------------|
| Reporting group title | Chemotherapy: Refractory |
|-----------------------|--------------------------|

Reporting group description:

Participants with disease not responding to prior chemotherapy received retifanlimab 500 mg, administered by IV infusion over 60 minutes on Day 1 Q4W.

|                       |       |
|-----------------------|-------|
| Reporting group title | Total |
|-----------------------|-------|

Reporting group description:

Total

| Serious adverse events  | Chemotherapy:<br>Naïve | Chemotherapy:<br>Refractory | Total             |
|---|------------------------|-----------------------------|-------------------|
| Total subjects affected by serious adverse events                   |                        |                             |                   |
| subjects affected / exposed   | 26 / 101 (25.74%)      | 2 / 6 (33.33%)              | 28 / 107 (26.17%) |
| number of deaths (all causes)                                       | 39                     | 3                           | 42                |
| number of deaths resulting from adverse events                      | 4                      | 0                           | 4                 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                        |                             |                   |
| Basal cell carcinoma  |                        |                             |                   |
| subjects affected / exposed   | 1 / 101 (0.99%)        | 0 / 6 (0.00%)               | 1 / 107 (0.93%)   |
| occurrences causally related to treatment / all                     | 0 / 1                  | 0 / 0                       | 0 / 1             |
| deaths causally related to treatment / all                          | 0 / 0                  | 0 / 0                       | 0 / 0             |
| Ductal adenocarcinoma of pancreas                                   |                        |                             |                   |
| subjects affected / exposed   | 1 / 101 (0.99%)        | 0 / 6 (0.00%)               | 1 / 107 (0.93%)   |
| occurrences causally related to treatment / all                     | 0 / 1                  | 0 / 0                       | 0 / 1             |
| deaths causally related to treatment / all                          | 0 / 0                  | 0 / 0                       | 0 / 0             |

|  |                 |                |                 |
|--|-----------------|----------------|-----------------|
| General disorders and administration site conditions |                 |                |                 |
| Asthenia   |                 |                |                 |
| subjects affected / exposed                          | 3 / 101 (2.97%) | 0 / 6 (0.00%)  | 3 / 107 (2.80%) |
| occurrences causally related to treatment / all      | 0 / 3           | 0 / 0          | 0 / 3           |
| deaths causally related to treatment / all           | 0 / 1           | 0 / 0          | 0 / 1           |
| Concomitant disease progression                      |                 |                |                 |
| subjects affected / exposed                          | 1 / 101 (0.99%) | 0 / 6 (0.00%)  | 1 / 107 (0.93%) |
| occurrences causally related to treatment / all      | 1 / 1           | 0 / 0          | 1 / 1           |
| deaths causally related to treatment / all           | 1 / 1           | 0 / 0          | 1 / 1           |
| Influenza like illness                               |                 |                |                 |
| subjects affected / exposed                          | 1 / 101 (0.99%) | 0 / 6 (0.00%)  | 1 / 107 (0.93%) |
| occurrences causally related to treatment / all      | 0 / 1           | 0 / 0          | 0 / 1           |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0          | 0 / 0           |
| Immune system disorders                              |                 |                |                 |
| Drug hypersensitivity                                |                 |                |                 |
| subjects affected / exposed                          | 1 / 101 (0.99%) | 0 / 6 (0.00%)  | 1 / 107 (0.93%) |
| occurrences causally related to treatment / all      | 1 / 2           | 0 / 0          | 1 / 2           |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0          | 0 / 0           |
| Respiratory, thoracic and mediastinal disorders      |                 |                |                 |
| Acute respiratory failure                            |                 |                |                 |
| subjects affected / exposed                          | 1 / 101 (0.99%) | 0 / 6 (0.00%)  | 1 / 107 (0.93%) |
| occurrences causally related to treatment / all      | 0 / 1           | 0 / 0          | 0 / 1           |
| deaths causally related to treatment / all           | 0 / 1           | 0 / 0          | 0 / 1           |
| Dyspnoea   |                 |                |                 |
| subjects affected / exposed                          | 0 / 101 (0.00%) | 1 / 6 (16.67%) | 1 / 107 (0.93%) |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 1          | 0 / 1           |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0          | 0 / 0           |
| Hypoxia  |                 |                |                 |
| subjects affected / exposed                          | 0 / 101 (0.00%) | 1 / 6 (16.67%) | 1 / 107 (0.93%) |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 1          | 0 / 1           |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0          | 0 / 0           |
| Lung disorder  |                 |                |                 |

|   |                 |               |                 |
|---|-----------------|---------------|-----------------|
| subjects affected / exposed                     | 1 / 101 (0.99%) | 0 / 6 (0.00%) | 1 / 107 (0.93%) |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0         | 1 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 0           |
| Organising pneumonia                            |                 |               |                 |
| subjects affected / exposed                     | 1 / 101 (0.99%) | 0 / 6 (0.00%) | 1 / 107 (0.93%) |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0         | 1 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 0           |
| Pulmonary embolism                              |                 |               |                 |
| subjects affected / exposed                     | 1 / 101 (0.99%) | 0 / 6 (0.00%) | 1 / 107 (0.93%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0         | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 0           |
| Pneumothorax                                    |                 |               |                 |
| subjects affected / exposed                     | 1 / 101 (0.99%) | 0 / 6 (0.00%) | 1 / 107 (0.93%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0         | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 0           |
| Pneumonitis                                     |                 |               |                 |
| subjects affected / exposed                     | 2 / 101 (1.98%) | 0 / 6 (0.00%) | 2 / 107 (1.87%) |
| occurrences causally related to treatment / all | 1 / 3           | 0 / 0         | 1 / 3           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 0           |
| Investigations                                  |                 |               |                 |
| Amylase increased                               |                 |               |                 |
| subjects affected / exposed                     | 1 / 101 (0.99%) | 0 / 6 (0.00%) | 1 / 107 (0.93%) |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0         | 1 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 0           |
| Lipase increased                                |                 |               |                 |
| subjects affected / exposed                     | 1 / 101 (0.99%) | 0 / 6 (0.00%) | 1 / 107 (0.93%) |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0         | 1 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 0           |
| Injury, poisoning and procedural complications  |                 |               |                 |
| Infusion related reaction                       |                 |               |                 |
| subjects affected / exposed                     | 1 / 101 (0.99%) | 0 / 6 (0.00%) | 1 / 107 (0.93%) |
| occurrences causally related to treatment / all | 2 / 2           | 0 / 0         | 2 / 2           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 0           |

|   |                 |                |                 |
|---|-----------------|----------------|-----------------|
| Spinal fracture                                 |                 |                |                 |
| subjects affected / exposed                     | 1 / 101 (0.99%) | 0 / 6 (0.00%)  | 1 / 107 (0.93%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0           |
| Cardiac disorders                               |                 |                |                 |
| Atrial fibrillation                             |                 |                |                 |
| subjects affected / exposed                     | 2 / 101 (1.98%) | 0 / 6 (0.00%)  | 2 / 107 (1.87%) |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 0          | 0 / 2           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0           |
| Acute myocardial infarction                     |                 |                |                 |
| subjects affected / exposed                     | 1 / 101 (0.99%) | 0 / 6 (0.00%)  | 1 / 107 (0.93%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0           |
| Cardiac failure                                 |                 |                |                 |
| subjects affected / exposed                     | 1 / 101 (0.99%) | 0 / 6 (0.00%)  | 1 / 107 (0.93%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0           |
| Atrioventricular block                          |                 |                |                 |
| subjects affected / exposed                     | 1 / 101 (0.99%) | 0 / 6 (0.00%)  | 1 / 107 (0.93%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0           |
| Pericardial effusion                            |                 |                |                 |
| subjects affected / exposed                     | 1 / 101 (0.99%) | 0 / 6 (0.00%)  | 1 / 107 (0.93%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0           |
| Nervous system disorders                        |                 |                |                 |
| Demyelinating polyneuropathy                    |                 |                |                 |
| subjects affected / exposed                     | 1 / 101 (0.99%) | 0 / 6 (0.00%)  | 1 / 107 (0.93%) |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0          | 1 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0           |
| Radiculopathy                                   |                 |                |                 |
| subjects affected / exposed                     | 0 / 101 (0.00%) | 1 / 6 (16.67%) | 1 / 107 (0.93%) |
| occurrences causally related to treatment / all | 0 / 0           | 1 / 1          | 1 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0           |



|   |                 |               |                 |
|---|-----------------|---------------|-----------------|
| Gastrointestinal disorders                      |                 |               |                 |
| Colitis   |                 |               |                 |
| subjects affected / exposed                     | 1 / 101 (0.99%) | 0 / 6 (0.00%) | 1 / 107 (0.93%) |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0         | 1 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 0           |
| Gastric haemorrhage                             |                 |               |                 |
| subjects affected / exposed                     | 1 / 101 (0.99%) | 0 / 6 (0.00%) | 1 / 107 (0.93%) |
| occurrences causally related to treatment / all | 1 / 2           | 0 / 0         | 1 / 2           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 0           |
| Pancreatitis                                    |                 |               |                 |
| subjects affected / exposed                     | 1 / 101 (0.99%) | 0 / 6 (0.00%) | 1 / 107 (0.93%) |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0         | 1 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 0           |
| Hepatobiliary disorders                         |                 |               |                 |
| Hepatitis                                       |                 |               |                 |
| subjects affected / exposed                     | 1 / 101 (0.99%) | 0 / 6 (0.00%) | 1 / 107 (0.93%) |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0         | 1 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 0           |
| Skin and subcutaneous tissue disorders          |                 |               |                 |
| Toxic epidermal necrolysis                      |                 |               |                 |
| subjects affected / exposed                     | 1 / 101 (0.99%) | 0 / 6 (0.00%) | 1 / 107 (0.93%) |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0         | 1 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 0           |
| Renal and urinary disorders                     |                 |               |                 |
| Hydronephrosis                                  |                 |               |                 |
| subjects affected / exposed                     | 1 / 101 (0.99%) | 0 / 6 (0.00%) | 1 / 107 (0.93%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0         | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 0           |
| Endocrine disorders                             |                 |               |                 |
| Adrenal insufficiency                           |                 |               |                 |
| subjects affected / exposed                     | 1 / 101 (0.99%) | 0 / 6 (0.00%) | 1 / 107 (0.93%) |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0         | 1 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 0           |
| Musculoskeletal and connective tissue disorders |                 |               |                 |
| Bone pain                                       |                 |               |                 |

|   |                 |               |                 |
|---|-----------------|---------------|-----------------|
| subjects affected / exposed                     | 2 / 101 (1.98%) | 0 / 6 (0.00%) | 2 / 107 (1.87%) |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 0         | 0 / 2           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 0           |
| Eosinophilic fasciitis                          |                 |               |                 |
| subjects affected / exposed                     | 1 / 101 (0.99%) | 0 / 6 (0.00%) | 1 / 107 (0.93%) |
| occurrences causally related to treatment / all | 2 / 2           | 0 / 0         | 2 / 2           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 0           |
| Infections and infestations                     |                 |               |                 |
| COVID-19  |                 |               |                 |
| subjects affected / exposed                     | 4 / 101 (3.96%) | 0 / 6 (0.00%) | 4 / 107 (3.74%) |
| occurrences causally related to treatment / all | 0 / 4           | 0 / 0         | 0 / 4           |
| deaths causally related to treatment / all      | 0 / 1           | 0 / 0         | 0 / 1           |
| Pneumonia                                       |                 |               |                 |
| subjects affected / exposed                     | 1 / 101 (0.99%) | 0 / 6 (0.00%) | 1 / 107 (0.93%) |
| occurrences causally related to treatment / all | 0 / 3           | 0 / 0         | 0 / 3           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 0           |
| Urinary tract infection                         |                 |               |                 |
| subjects affected / exposed                     | 2 / 101 (1.98%) | 0 / 6 (0.00%) | 2 / 107 (1.87%) |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 0         | 0 / 2           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 0           |
| Sepsis  |                 |               |                 |
| subjects affected / exposed                     | 1 / 101 (0.99%) | 0 / 6 (0.00%) | 1 / 107 (0.93%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0         | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 0           |
| Metabolism and nutrition disorders              |                 |               |                 |
| Diabetic ketoacidosis                           |                 |               |                 |
| subjects affected / exposed                     | 1 / 101 (0.99%) | 0 / 6 (0.00%) | 1 / 107 (0.93%) |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0         | 1 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 0           |
| Hyponatraemia                                   |                 |               |                 |
| subjects affected / exposed                     | 1 / 101 (0.99%) | 0 / 6 (0.00%) | 1 / 107 (0.93%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0         | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 0           |
| Hypoglycaemia                                   |                 |               |                 |

|   |                 |               |                 |
|---|-----------------|---------------|-----------------|
| subjects affected / exposed                     | 1 / 101 (0.99%) | 0 / 6 (0.00%) | 1 / 107 (0.93%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0         | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 0           |

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

| <b>Non-serious adverse events</b>                     | Chemotherapy:<br>Naïve | Chemotherapy:<br>Refractory | Total             |
|---|------------------------|-----------------------------|-------------------|
| Total subjects affected by non-serious adverse events |                        |                             |                   |
| subjects affected / exposed                           | 83 / 101 (82.18%)      | 5 / 6 (83.33%)              | 88 / 107 (82.24%) |
| Vascular disorders                                    |                        |                             |                   |
| Hypertension  |                        |                             |                   |
| subjects affected / exposed                           | 7 / 101 (6.93%)        | 1 / 6 (16.67%)              | 8 / 107 (7.48%)   |
| occurrences (all)                                     | 7                      | 1                           | 8                 |
| Hypotension   |                        |                             |                   |
| subjects affected / exposed                           | 2 / 101 (1.98%)        | 1 / 6 (16.67%)              | 3 / 107 (2.80%)   |
| occurrences (all)                                     | 2                      | 1                           | 3                 |
| General disorders and administration site conditions  |                        |                             |                   |
| Asthenia  |                        |                             |                   |
| subjects affected / exposed                           | 19 / 101 (18.81%)      | 2 / 6 (33.33%)              | 21 / 107 (19.63%) |
| occurrences (all)                                     | 24                     | 3                           | 27                |
| Fatigue   |                        |                             |                   |
| subjects affected / exposed                           | 10 / 101 (9.90%)       | 3 / 6 (50.00%)              | 13 / 107 (12.15%) |
| occurrences (all)                                     | 12                     | 3                           | 15                |
| Oedema peripheral                                     |                        |                             |                   |
| subjects affected / exposed                           | 7 / 101 (6.93%)        | 0 / 6 (0.00%)               | 7 / 107 (6.54%)   |
| occurrences (all)                                     | 7                      | 0                           | 7                 |
| Pyrexia   |                        |                             |                   |
| subjects affected / exposed                           | 11 / 101 (10.89%)      | 2 / 6 (33.33%)              | 13 / 107 (12.15%) |
| occurrences (all)                                     | 14                     | 5                           | 19                |
| Reproductive system and breast disorders              |                        |                             |                   |
| Gynaecomastia   |                        |                             |                   |
| subjects affected / exposed                           | 0 / 101 (0.00%)        | 1 / 6 (16.67%)              | 1 / 107 (0.93%)   |
| occurrences (all)                                     | 0                      | 1                           | 1                 |
| Respiratory, thoracic and mediastinal disorders       |                        |                             |                   |

|  |                        |                     |                        |
|--|------------------------|---------------------|------------------------|
| Cough<br>subjects affected / exposed<br>occurrences (all)  | 10 / 101 (9.90%)<br>11 | 0 / 6 (0.00%)<br>0  | 10 / 107 (9.35%)<br>11 |
| Nasal congestion<br>subjects affected / exposed<br>occurrences (all)                                       | 1 / 101 (0.99%)<br>1   | 1 / 6 (16.67%)<br>1 | 2 / 107 (1.87%)<br>2   |
| Nasal turbinate hypertrophy<br>subjects affected / exposed<br>occurrences (all)                            | 0 / 101 (0.00%)<br>0   | 1 / 6 (16.67%)<br>1 | 1 / 107 (0.93%)<br>1   |
| Pleural effusion<br>subjects affected / exposed<br>occurrences (all)                                       | 0 / 101 (0.00%)<br>0   | 1 / 6 (16.67%)<br>1 | 1 / 107 (0.93%)<br>1   |
| Psychiatric disorders<br>Insomnia<br>subjects affected / exposed<br>occurrences (all)                      | 6 / 101 (5.94%)<br>6   | 0 / 6 (0.00%)<br>0  | 6 / 107 (5.61%)<br>6   |
| Investigations<br>Aspartate aminotransferase increased<br>subjects affected / exposed<br>occurrences (all) | 6 / 101 (5.94%)<br>6   | 1 / 6 (16.67%)<br>1 | 7 / 107 (6.54%)<br>7   |
| Alanine aminotransferase increased<br>subjects affected / exposed<br>occurrences (all)                     | 8 / 101 (7.92%)<br>8   | 0 / 6 (0.00%)<br>0  | 8 / 107 (7.48%)<br>8   |
| Amylase increased<br>subjects affected / exposed<br>occurrences (all)                                      | 8 / 101 (7.92%)<br>11  | 0 / 6 (0.00%)<br>0  | 8 / 107 (7.48%)<br>11  |
| Blood creatinine increased<br>subjects affected / exposed<br>occurrences (all)                             | 7 / 101 (6.93%)<br>7   | 1 / 6 (16.67%)<br>1 | 8 / 107 (7.48%)<br>8   |
| Blood lactate dehydrogenase increased<br>subjects affected / exposed<br>occurrences (all)                  | 2 / 101 (1.98%)<br>2   | 1 / 6 (16.67%)<br>1 | 3 / 107 (2.80%)<br>3   |
| Lipase increased<br>subjects affected / exposed<br>occurrences (all)                                       | 9 / 101 (8.91%)<br>11  | 0 / 6 (0.00%)<br>0  | 9 / 107 (8.41%)<br>11  |
| Low density lipoprotein increased  |                        |                     |                        |

|   |  |  |  |
|---|--|--|--|
| subjects affected / exposed<br>occurrences (all)  | 1 / 101 (0.99%)<br>1   | 1 / 6 (16.67%)<br>1  | 2 / 107 (1.87%)<br>2   |
| Injury, poisoning and procedural complications<br>Fall<br>subjects affected / exposed<br>occurrences (all)  | 0 / 101 (0.00%)<br>0   | 2 / 6 (33.33%)<br>2  | 2 / 107 (1.87%)<br>2   |
| Nervous system disorders<br>Paraesthesia<br>subjects affected / exposed<br>occurrences (all)<br><br>Tremor<br>subjects affected / exposed<br>occurrences (all)  | 2 / 101 (1.98%)<br>2<br><br>0 / 101 (0.00%)<br>0   | 1 / 6 (16.67%)<br>1<br><br>1 / 6 (16.67%)<br>1   | 3 / 107 (2.80%)<br>3<br><br>1 / 107 (0.93%)<br>1   |
| Blood and lymphatic system disorders<br>Anaemia<br>subjects affected / exposed<br>occurrences (all)   | 6 / 101 (5.94%)<br>6   | 1 / 6 (16.67%)<br>1  | 7 / 107 (6.54%)<br>7   |
| Eye disorders<br>Glaucoma<br>subjects affected / exposed<br>occurrences (all)   | 0 / 101 (0.00%)<br>0   | 1 / 6 (16.67%)<br>1  | 1 / 107 (0.93%)<br>1   |
| Gastrointestinal disorders<br>Constipation<br>subjects affected / exposed<br>occurrences (all)<br><br>Dyspepsia<br>subjects affected / exposed<br>occurrences (all)<br><br>Dry mouth<br>subjects affected / exposed<br>occurrences (all)<br><br>Diarrhoea<br>subjects affected / exposed<br>occurrences (all)<br><br>Nausea | 12 / 101 (11.88%)<br>13<br><br>4 / 101 (3.96%)<br>6<br><br>6 / 101 (5.94%)<br>6<br><br>19 / 101 (18.81%)<br>33 | 0 / 6 (0.00%)<br>0<br><br>1 / 6 (16.67%)<br>1<br><br>0 / 6 (0.00%)<br>0<br><br>1 / 6 (16.67%)<br>1 | 12 / 107 (11.21%)<br>13<br><br>5 / 107 (4.67%)<br>7<br><br>6 / 107 (5.61%)<br>6<br><br>20 / 107 (18.69%)<br>34 |

|   |                         |                     |                         |
|---|-------------------------|---------------------|-------------------------|
| subjects affected / exposed<br>occurrences (all)                    | 10 / 101 (9.90%)<br>11  | 3 / 6 (50.00%)<br>3 | 13 / 107 (12.15%)<br>14 |
| Toothache<br>subjects affected / exposed<br>occurrences (all)       | 0 / 101 (0.00%)<br>0    | 1 / 6 (16.67%)<br>1 | 1 / 107 (0.93%)<br>1    |
| Stomatitis<br>subjects affected / exposed<br>occurrences (all)      | 4 / 101 (3.96%)<br>4    | 1 / 6 (16.67%)<br>1 | 5 / 107 (4.67%)<br>5    |
| Vomiting<br>subjects affected / exposed<br>occurrences (all)        | 5 / 101 (4.95%)<br>5    | 1 / 6 (16.67%)<br>1 | 6 / 107 (5.61%)<br>6    |
| Skin and subcutaneous tissue disorders                              |                         |                     |                         |
| Hyperkeratosis<br>subjects affected / exposed<br>occurrences (all)  | 1 / 101 (0.99%)<br>1    | 1 / 6 (16.67%)<br>1 | 2 / 107 (1.87%)<br>2    |
| Erythema<br>subjects affected / exposed<br>occurrences (all)        | 6 / 101 (5.94%)<br>6    | 0 / 6 (0.00%)<br>0  | 6 / 107 (5.61%)<br>6    |
| Rash<br>subjects affected / exposed<br>occurrences (all)            | 7 / 101 (6.93%)<br>8    | 0 / 6 (0.00%)<br>0  | 7 / 107 (6.54%)<br>8    |
| Pruritus<br>subjects affected / exposed<br>occurrences (all)        | 22 / 101 (21.78%)<br>26 | 1 / 6 (16.67%)<br>1 | 23 / 107 (21.50%)<br>27 |
| Endocrine disorders   |                         |                     |                         |
| Hypothyroidism<br>subjects affected / exposed<br>occurrences (all)  | 8 / 101 (7.92%)<br>8    | 2 / 6 (33.33%)<br>2 | 10 / 107 (9.35%)<br>10  |
| Hypophysitis<br>subjects affected / exposed<br>occurrences (all)    | 1 / 101 (0.99%)<br>1    | 1 / 6 (16.67%)<br>1 | 2 / 107 (1.87%)<br>2    |
| Hyperthyroidism<br>subjects affected / exposed<br>occurrences (all) | 6 / 101 (5.94%)<br>6    | 0 / 6 (0.00%)<br>0  | 6 / 107 (5.61%)<br>6    |
| Musculoskeletal and connective tissue disorders                     |                         |                     |                         |

|                                    |                   |                |                   |
|------------------------------------|-------------------|----------------|-------------------|
| Arthralgia                         |                   |                |                   |
| subjects affected / exposed        | 17 / 101 (16.83%) | 2 / 6 (33.33%) | 19 / 107 (17.76%) |
| occurrences (all)                  | 23                | 5              | 28                |
| Back pain                          |                   |                |                   |
| subjects affected / exposed        | 5 / 101 (4.95%)   | 2 / 6 (33.33%) | 7 / 107 (6.54%)   |
| occurrences (all)                  | 5                 | 2              | 7                 |
| Groin pain                         |                   |                |                   |
| subjects affected / exposed        | 0 / 101 (0.00%)   | 1 / 6 (16.67%) | 1 / 107 (0.93%)   |
| occurrences (all)                  | 0                 | 1              | 1                 |
| Muscle spasms                      |                   |                |                   |
| subjects affected / exposed        | 2 / 101 (1.98%)   | 1 / 6 (16.67%) | 3 / 107 (2.80%)   |
| occurrences (all)                  | 2                 | 1              | 3                 |
| Myalgia                            |                   |                |                   |
| subjects affected / exposed        | 5 / 101 (4.95%)   | 2 / 6 (33.33%) | 7 / 107 (6.54%)   |
| occurrences (all)                  | 5                 | 3              | 8                 |
| Pain in extremity                  |                   |                |                   |
| subjects affected / exposed        | 4 / 101 (3.96%)   | 1 / 6 (16.67%) | 5 / 107 (4.67%)   |
| occurrences (all)                  | 4                 | 1              | 5                 |
| Infections and infestations        |                   |                |                   |
| Conjunctivitis                     |                   |                |                   |
| subjects affected / exposed        | 5 / 101 (4.95%)   | 1 / 6 (16.67%) | 6 / 107 (5.61%)   |
| occurrences (all)                  | 5                 | 1              | 6                 |
| COVID-19                           |                   |                |                   |
| subjects affected / exposed        | 10 / 101 (9.90%)  | 0 / 6 (0.00%)  | 10 / 107 (9.35%)  |
| occurrences (all)                  | 11                | 0              | 11                |
| Oral candidiasis                   |                   |                |                   |
| subjects affected / exposed        | 0 / 101 (0.00%)   | 1 / 6 (16.67%) | 1 / 107 (0.93%)   |
| occurrences (all)                  | 0                 | 1              | 1                 |
| Urinary tract infection            |                   |                |                   |
| subjects affected / exposed        | 5 / 101 (4.95%)   | 1 / 6 (16.67%) | 6 / 107 (5.61%)   |
| occurrences (all)                  | 9                 | 1              | 10                |
| Metabolism and nutrition disorders |                   |                |                   |
| Decreased appetite                 |                   |                |                   |
| subjects affected / exposed        | 6 / 101 (5.94%)   | 0 / 6 (0.00%)  | 6 / 107 (5.61%)   |
| occurrences (all)                  | 6                 | 0              | 6                 |
| Dehydration                        |                   |                |                   |

|                             |                 |                |                 |
|-----------------------------|-----------------|----------------|-----------------|
| subjects affected / exposed | 1 / 101 (0.99%) | 1 / 6 (16.67%) | 2 / 107 (1.87%) |
| occurrences (all)           | 1               | 1              | 2               |
| Hyponatraemia               |                 |                |                 |
| subjects affected / exposed | 1 / 101 (0.99%) | 1 / 6 (16.67%) | 2 / 107 (1.87%) |
| occurrences (all)           | 6               | 1              | 7               |



## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date             | Amendment  |
|------------------|--|
| 27 June 2018     | The primary purpose of this amendment was to address comments received from the United States Food and Drug Administration.  |
| 04 October 2018  | The primary purpose of this amendment was to address comments received from the European Competent Authorities during the Voluntary Harmonization Procedure.   |
| 05 December 2018 | The primary purpose of this amendment was to address comments received from Health Canada. Additional clarifications and administrative changes were also made.  |
| 16 August 2019   | The primary purpose of this amendment was to expand the eligibility criteria to include participants with recurrent locoregional advanced disease in addition to participants with distant metastatic Merkel cell carcinoma.         |
| 09 April 2020    | The primary purpose of this amendment was to clarify the definition of target lesions for participants who had progression in areas previously treated with locoregional therapy.  |
| 22 October 2020  | The primary purpose of this amendment was to increase the sample size of the study to allow for more robust characterization of the primary and secondary endpoints.   |
| 16 December 2021 | The primary purpose of this amendment was to update immune-related adverse event management guidelines to reflect updated published guidance and to provide guidance on the management of participants during the COVID-19 pandemic. |
| 18 May 2023      | The primary purpose of this amendment was to update the definition of the end of the study.  |

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported