



## Clinical trial results:

### A Phase 2 Study of INCMGA00012 in Participants With Squamous Carcinoma of the Anal Canal Who Have Progressed Following Platinum-Based Chemotherapy (POD1UM 202)

#### Summary

|                          |                      |
|--------------------------|----------------------|
| EudraCT number           | 2018-002070-51       |
| Trial protocol           | NL BE GB DE IT DK FR |
| Global end of trial date | 10 November 2021     |

#### Results information

|                                |                  |
|--------------------------------|------------------|
| Result version number          | v1 (current)     |
| This version publication date  | 15 December 2022 |
| First version publication date | 15 December 2022 |

#### Trial information

##### Trial identification

|                       |                 |
|-----------------------|-----------------|
| Sponsor protocol code | INCMGA 0012-202 |
|-----------------------|-----------------|

##### 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 Drive, 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                       | 10 November 2021 |
| Is this the analysis of the primary completion data? | No               |
| Global end of trial reached?                         | Yes              |
| Global end of trial date                             | 10 November 2021 |
| Was the trial ended prematurely?                     | No               |

Notes:

## General information about the trial

Main objective of the trial:

The purpose of this study was to assess the efficacy of retifanlimab in participants with locally advanced or metastatic squamous carcinoma of the anal canal (SCAC) who progressed after platinum-based chemotherapy.

Protection of trial subjects:

This study was to be performed in accordance with ethical principles that have their origin in the Declaration of Helsinki and conducted in adherence to the study Protocol, applicable Good Clinical Practices, and applicable laws and country-specific regulations in which the study was being conducted. The research in the Netherlands was carried out in accordance with the Declaration of Helsinki (Brazil, 2013) and the WMO (Medical Research Involving Human Subjects Act).

Background therapy: -

Evidence for comparator: -

|   |                 |
|---|-----------------|
| Actual start date of recruitment                          | 08 October 2018 |
| 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 | Belgium: 4         |
| Country: Number of subjects enrolled | Germany: 2         |
| Country: Number of subjects enrolled | Denmark: 7         |
| Country: Number of subjects enrolled | Spain: 10          |
| Country: Number of subjects enrolled | France: 32         |
| Country: Number of subjects enrolled | United Kingdom: 19 |
| Country: Number of subjects enrolled | Italy: 10          |
| Country: Number of subjects enrolled | Norway: 4          |
| Country: Number of subjects enrolled | United States: 6   |
| Worldwide total number of subjects   | 94                 |
| EEA total number of subjects         | 69                 |

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)                     | 48 |
| From 65 to 84 years                      | 45 |
| 85 years and over                        | 1  |

## Subject disposition

### Recruitment

Recruitment details:

This study was conducted at 40 study centers: 32 in France, 19 in the United Kingdom, 10 in Italy, 10 in Spain, 7 in Denmark, 6 in the United States, 4 in Norway, 4 in Belgium, and 2 in Germany.

### Pre-assignment

Screening details:

A total of 94 participants with locally advanced or metastatic squamous carcinoma of the anal canal were enrolled in the study and treated with retifanlimab.

### Period 1

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

### Arms

|           |                     |
|-----------|---------------------|
| Arm title | Retifanlimab 500 mg |
|-----------|---------------------|

Arm description:

Participants received retifanlimab 500 milligrams (mg) intravenously every 4 weeks (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:

retifanlimab 500 milligrams (mg) every 4 weeks (Q4W)

|                                       |                     |
|---------------------------------------|---------------------|
| <b>Number of subjects in period 1</b> | Retifanlimab 500 mg |
| Started                               | 94                  |
| Completed                             | 17                  |
| Not completed                         | 77                  |
| Adverse event, serious fatal          | 70                  |
| Lost to follow-up                     | 7                   |

## Baseline characteristics

### Reporting groups

|                       |                     |
|-----------------------|---------------------|
| Reporting group title | Retifanlimab 500 mg |
|-----------------------|---------------------|

Reporting group description:

Participants received retifanlimab 500 milligrams (mg) intravenously every 4 weeks (Q4W).

| Reporting group values                             | Retifanlimab 500 mg | Total |  |
|--|---------------------|-------|--|
| Number of subjects                                 | 94                  | 94    |  |
| Age categorical                                    |                     |       |  |
| Units: Subjects                                    |                     |       |  |
| In utero   | 0                   | 0     |  |
| Preterm newborn infants (gestational age < 37 wks) | 0                   | 0     |  |
| Newborns (0-27 days)                               | 0                   | 0     |  |
| Infants and toddlers (28 days-23 months)           | 0                   | 0     |  |
| Children (2-11 years)                              | 0                   | 0     |  |
| Adolescents (12-17 years)                          | 0                   | 0     |  |
| Adults (18-64 years)                               | 48                  | 48    |  |
| From 65-84 years                                   | 45                  | 45    |  |
| 85 years and over                                  | 1                   | 1     |  |
| Age Continuous                                     |                     |       |  |
| Units: Years                                       |                     |       |  |
| arithmetic mean                                    | 62.1                |       |  |
| standard deviation                                 | ± 11.44             | -     |  |
| Sex: Female, Male                                  |                     |       |  |
| Units:   |                     |       |  |
| Female   | 61                  | 61    |  |
| Male   | 33                  | 33    |  |
| Ethnicity, Customized                              |                     |       |  |
| Units: Subjects                                    |                     |       |  |
| Hispanic or Latino                                 | 4                   | 4     |  |
| Not Hispanic or Latino                             | 49                  | 49    |  |
| Not Reported                                       | 33                  | 33    |  |
| Unknown  | 4                   | 4     |  |
| Missing  | 4                   | 4     |  |
| Race, Customized                                   |                     |       |  |
| Units: Subjects                                    |                     |       |  |
| White/Caucasian                                    | 72                  | 72    |  |
| Black/African-American                             | 1                   | 1     |  |
| Captured as "Other"                                | 4                   | 4     |  |
| Missing  | 6                   | 6     |  |
| Not Reported                                       | 11                  | 11    |  |

## End points

### End points reporting groups

|   |                     |
|---|---------------------|
| Reporting group title   | Retifanlimab 500 mg |
| Reporting group description:  |                     |
| Participants received retifanlimab 500 milligrams (mg) intravenously every 4 weeks (Q4W). |                     |

### Primary: Objective response rate (ORR)

|  |  |
|--|--|
| End point title  | Objective response rate (ORR) <sup>[1]</sup> |
| End point description:   |  |
| ORR was defined as the percentage of participants with a best overall response of complete response (CR) or partial response (PR), per Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1 (v1.1), as assessed by independent central radiographic (ICR) review, at any post-Baseline visit until new anti-cancer therapy or first Progressive Disease. 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 millimeters (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. |  |
| End point type   | Primary                                      |
| End point timeframe:   |  |
| Cycle 1 Day 1, and every 4 weeks throughout the study, up to approximately 24 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.

|                                   |                     |  |  |  |
|-----------------------------------|---------------------|--|--|--|
| End point values                  | Retifanlimab 500 mg |  |  |  |
| Subject group type                | Reporting group     |  |  |  |
| Number of subjects analysed       | 94 <sup>[2]</sup>   |  |  |  |
| Units: percentage of participants |                     |  |  |  |
| number (not applicable)           | 13.8                |  |  |  |

Notes:

[2] - Full Analysis Set: all participants enrolled in the study who received at least 1 dose of study drug

### 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 was defined as the time from an initial objective response (CR or PR) per RECIST v1.1 until the first observation of documented disease progression (PD), as determined by ICR, or death due to any cause. 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. 9999=the upper limit of the confidence interval was not estimable because too few participants had disease progression or died. The 95% confidence interval was calculated using the Brookmeyer and Crowley's method and Klein and Moeschberger's method with log-log transformation. |                            |
| End point type  | Secondary                  |

End point timeframe:  
up to 18.2 months

|                                  |                        |  |  |  |
|----------------------------------|------------------------|--|--|--|
| <b>End point values</b>          | Retifanlimab<br>500 mg |  |  |  |
| Subject group type               | Reporting group        |  |  |  |
| Number of subjects analysed      | 13 <sup>[3]</sup>      |  |  |  |
| Units: months                    |                        |  |  |  |
| median (confidence interval 95%) | 9.5 (4.4 to<br>9999)   |  |  |  |

Notes:

[3] - Full Analysis Set. Participants with confirmed CR or PR by ICR per RECIST v1.1 were analyzed.

## 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 of CR, PR, or stable disease (SD), per RECIST v1.1, at any post-baseline visit until the first progressive disease (PD) or new anti-cancer therapy. 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. Confidence intervals were calculated based on the exact method for binomial distributions.

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

End point timeframe:

Cycle 1 Day 1, and every 4 weeks throughout the study, up to approximately 24 months

|                                   |                        |  |  |  |
|-----------------------------------|------------------------|--|--|--|
| <b>End point values</b>           | Retifanlimab<br>500 mg |  |  |  |
| Subject group type                | Reporting group        |  |  |  |
| Number of subjects analysed       | 94 <sup>[4]</sup>      |  |  |  |
| Units: percentage of participants |                        |  |  |  |
| number (confidence interval 95%)  | 48.9 (38.5 to<br>59.5) |  |  |  |

Notes:

[4] - Full Analysis Set

## 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 RECIST 1.1, PFS was defined as the length of time from the initial infusion of study drug until the earliest date of disease progression, as determined by ICR, or death due to any cause, if occurring sooner than progression. Median PFS time was estimated using the Kaplan-Meier method. The confidence interval for median PFS time was calculated using the method of Brookmeyer and Crowley. |                                 |
| End point type  | Secondary                       |
| End point timeframe:  |                                 |
| up to 16.8 months   |                                 |

|                                  |                        |  |  |  |
|----------------------------------|------------------------|--|--|--|
| <b>End point values</b>          | Retifanlimab<br>500 mg |  |  |  |
| Subject group type               | Reporting group        |  |  |  |
| Number of subjects analysed      | 94 <sup>[5]</sup>      |  |  |  |
| Units: months                    |                        |  |  |  |
| median (confidence interval 95%) | 2.3 (1.9 to 3.6)       |  |  |  |

Notes:

[5] - Full Analysis Set

### 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. Median survival time was estimated using the Kaplan-Meier method. The confidence interval for median survival time was calculated using the method of Brookmeyer and Crowley. |                  |
| End point type   | Secondary        |
| End point timeframe:   |                  |
| up to 28.2 months  |                  |

|                                  |                        |  |  |  |
|----------------------------------|------------------------|--|--|--|
| <b>End point values</b>          | Retifanlimab<br>500 mg |  |  |  |
| Subject group type               | Reporting group        |  |  |  |
| Number of subjects analysed      | 94 <sup>[6]</sup>      |  |  |  |
| Units: months                    |                        |  |  |  |
| median (confidence interval 95%) | 13.4 (10.1 to 15.0)    |  |  |  |

Notes:

[6] - Full Analysis Set

### Statistical analyses

No statistical analyses for this end point



## Secondary: Cmax of retifanlimab

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

End point description:

Cmax was defined as the maximum observed plasma concentration. Pharmacokinetic (PK) Evaluable Population: all participants who received at least 1 dose of study drug and provided a Baseline and at least 1 postdose serum sample (1 PK measurement).

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

End point timeframe:

pre-infusion on Day 1 of Cycles 1, 2, 4, 6, and 7; 10 minutes and 4 hours post-infusion on Day 1 of Cycles 1 and 6

|                                      |                        |  |  |  |
|--------------------------------------|------------------------|--|--|--|
| <b>End point values</b>              | Retifanlimab<br>500 mg |  |  |  |
| Subject group type                   | Reporting group        |  |  |  |
| Number of subjects analysed          | 92 <sup>[7]</sup>      |  |  |  |
| Units: milligrams per Liter (mg/L)   |                        |  |  |  |
| arithmetic mean (standard deviation) | 151 (± 27.6)           |  |  |  |

Notes:

[7] - PK Evaluable Population

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of participants with treatment-emergent adverse events (TEAEs)

|                 |   |
|-----------------|---|
| End point title | Number of participants with treatment-emergent adverse events (TEAEs) |
|-----------------|---|

End point description:

An adverse event (AE) was defined as any untoward medical occurrence associated with the use of a drug in humans, whether or not considered drug-related. An AE could have been any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease (new or exacerbated) temporally associated with the use of the study drug. A TEAE was defined as any AE either reported for the first time or the worsening of a pre-existing event after the first dose of retifanlimab and within 90 days of the last administration of retifanlimab.

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

End point timeframe:

up to 913 days

|                             |                        |  |  |  |
|-----------------------------|------------------------|--|--|--|
| <b>End point values</b>     | Retifanlimab<br>500 mg |  |  |  |
| Subject group type          | Reporting group        |  |  |  |
| Number of subjects analysed | 94 <sup>[8]</sup>      |  |  |  |
| Units: participants         | 90                     |  |  |  |

Notes:

[8] - Safety Evaluable Population: all enrolled participants who received at least 1 dose of study drug

## Statistical analyses

No statistical analyses for this end point

### Secondary: tmax of retifanlimab

|                 |                      |
|-----------------|----------------------|
| End point title | tmax of retifanlimab |
|-----------------|----------------------|

End point description:

tmax was defined as the time to the maximum concentration.

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

End point timeframe:

pre-infusion on Day 1 of Cycles 1, 2, 4, 6, and 7; 10 minutes and 4 hours post-infusion on Day 1 of Cycles 1 and 6

| End point values                     | Retifanlimab<br>500 mg |  |  |  |
|--------------------------------------|------------------------|--|--|--|
| Subject group type                   | Reporting group        |  |  |  |
| Number of subjects analysed          | 92 <sup>[9]</sup>      |  |  |  |
| Units: hours                         |                        |  |  |  |
| arithmetic mean (standard deviation) | 1.20 (± 0.305)         |  |  |  |

Notes:

[9] - PK Evaluable Population

### Statistical analyses

No statistical analyses for this end point

### Secondary: Cmin of retifanlimab

|                 |                      |
|-----------------|----------------------|
| End point title | 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:

pre-infusion on Day 1 of Cycles 1, 2, 4, 6, and 7; 10 minutes and 4 hours post-infusion on Day 1 of Cycles 1 and 6

| End point values                     | Retifanlimab<br>500 mg |  |  |  |
|--------------------------------------|------------------------|--|--|--|
| Subject group type                   | Reporting group        |  |  |  |
| Number of subjects analysed          | 92 <sup>[10]</sup>     |  |  |  |
| Units: mg/L                          |                        |  |  |  |
| arithmetic mean (standard deviation) | 22.4 (± 7.87)          |  |  |  |

Notes:

[10] - PK Evaluable Population

### Statistical analyses

No statistical analyses for this end point

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**Secondary: AUC0-t of retifanlimab**

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

End point description:

AUC0-t was defined as the area under the plasma concentration-time curve from time = 0 to the last measurable concentration at time = t.

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

End point timeframe:

pre-infusion on Day 1 of Cycles 1, 2, 4, 6, and 7; 10 minutes and 4 hours post-infusion on Day 1 of Cycles 1 and 6

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|                                      |                        |  |  |  |
|--------------------------------------|------------------------|--|--|--|
| <b>End point values</b>              | Retifanlimab<br>500 mg |  |  |  |
| Subject group type                   | Reporting group        |  |  |  |
| Number of subjects analysed          | 92 <sup>[11]</sup>     |  |  |  |
| Units: day*mg/L                      |                        |  |  |  |
| arithmetic mean (standard deviation) | 1950 (± 594)           |  |  |  |

Notes:

[11] - 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:

up to 913 days

Adverse event reporting additional description:

Treatment-emergent adverse events (TEAEs), defined as any AEs either reported for the first time or the worsening of pre-existing events after the first dose of retifanlimab and within 90 days of the last administration of retifanlimab, have been reported.

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

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 23.1 |
|--------------------|------|

### Reporting groups

|                       |                     |
|-----------------------|---------------------|
| Reporting group title | Retifanlimab 500 mg |
|-----------------------|---------------------|

Reporting group description:

Participants received retifanlimab 500 milligrams (mg) intravenously every 4 weeks (Q4W).

| Serious adverse events  | Retifanlimab 500 mg |  |  |
|---|---------------------|--|--|
| Total subjects affected by serious adverse events                   |                     |  |  |
| subjects affected / exposed   | 50 / 94 (53.19%)    |  |  |
| number of deaths (all causes)                                       | 60                  |  |  |
| number of deaths resulting from adverse events                      | 10                  |  |  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                     |  |  |
| Diffuse large B-cell lymphoma                                       |                     |  |  |
| subjects affected / exposed   | 1 / 94 (1.06%)      |  |  |
| occurrences causally related to treatment / all                     | 0 / 1               |  |  |
| deaths causally related to treatment / all                          | 0 / 0               |  |  |
| Pancreatic carcinoma  |                     |  |  |
| subjects affected / exposed   | 1 / 94 (1.06%)      |  |  |
| occurrences causally related to treatment / all                     | 0 / 1               |  |  |
| deaths causally related to treatment / all                          | 0 / 1               |  |  |
| Lymphangiosis carcinomatosa   |                     |  |  |
| subjects affected / exposed   | 1 / 94 (1.06%)      |  |  |
| occurrences causally related to treatment / all                     | 1 / 1               |  |  |
| deaths causally related to treatment / all                          | 1 / 1               |  |  |
| Transitional cell carcinoma   |                     |  |  |

|  |                |  |  |
|--|----------------|--|--|
| subjects affected / exposed                          | 1 / 94 (1.06%) |  |  |
| occurrences causally related to treatment / all      | 0 / 1          |  |  |
| deaths causally related to treatment / all           | 0 / 0          |  |  |
| Tumour embolism                                      |                |  |  |
| subjects affected / exposed                          | 1 / 94 (1.06%) |  |  |
| occurrences causally related to treatment / all      | 0 / 1          |  |  |
| deaths causally related to treatment / all           | 0 / 1          |  |  |
| Tumour pain  |                |  |  |
| subjects affected / exposed                          | 1 / 94 (1.06%) |  |  |
| occurrences causally related to treatment / all      | 0 / 1          |  |  |
| deaths causally related to treatment / all           | 0 / 0          |  |  |
| Vascular disorders                                   |                |  |  |
| Thrombosis   |                |  |  |
| subjects affected / exposed                          | 1 / 94 (1.06%) |  |  |
| occurrences causally related to treatment / all      | 0 / 1          |  |  |
| deaths causally related to treatment / all           | 0 / 0          |  |  |
| Venous thrombosis limb                               |                |  |  |
| subjects affected / exposed                          | 1 / 94 (1.06%) |  |  |
| occurrences causally related to treatment / all      | 0 / 1          |  |  |
| deaths causally related to treatment / all           | 0 / 0          |  |  |
| General disorders and administration site conditions |                |  |  |
| Asthenia   |                |  |  |
| subjects affected / exposed                          | 1 / 94 (1.06%) |  |  |
| occurrences causally related to treatment / all      | 0 / 1          |  |  |
| deaths causally related to treatment / all           | 0 / 0          |  |  |
| Catheter site pain                                   |                |  |  |
| subjects affected / exposed                          | 1 / 94 (1.06%) |  |  |
| occurrences causally related to treatment / all      | 0 / 1          |  |  |
| deaths causally related to treatment / all           | 0 / 0          |  |  |
| General physical health deterioration                |                |  |  |
| subjects affected / exposed                          | 3 / 94 (3.19%) |  |  |
| occurrences causally related to treatment / all      | 0 / 3          |  |  |
| deaths causally related to treatment / all           | 0 / 0          |  |  |

|   |                |  |  |
|---|----------------|--|--|
| Inadequate analgesia                            |                |  |  |
| subjects affected / exposed                     | 2 / 94 (2.13%) |  |  |
| occurrences causally related to treatment / all | 0 / 2          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Pain  |                |  |  |
| subjects affected / exposed                     | 1 / 94 (1.06%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Pyrexia   |                |  |  |
| subjects affected / exposed                     | 3 / 94 (3.19%) |  |  |
| occurrences causally related to treatment / all | 0 / 3          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Reproductive system and breast disorders        |                |  |  |
| Pelvic pain                                     |                |  |  |
| subjects affected / exposed                     | 3 / 94 (3.19%) |  |  |
| occurrences causally related to treatment / all | 0 / 3          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Respiratory, thoracic and mediastinal disorders |                |  |  |
| Acute respiratory failure                       |                |  |  |
| subjects affected / exposed                     | 1 / 94 (1.06%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Dyspnoea  |                |  |  |
| subjects affected / exposed                     | 2 / 94 (2.13%) |  |  |
| occurrences causally related to treatment / all | 0 / 2          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Interstitial lung disease                       |                |  |  |
| subjects affected / exposed                     | 1 / 94 (1.06%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 1          |  |  |
| Pleural effusion                                |                |  |  |

|   |                |  |  |
|---|----------------|--|--|
| subjects affected / exposed                     | 2 / 94 (2.13%) |  |  |
| occurrences causally related to treatment / all | 0 / 3          |  |  |
| deaths causally related to treatment / all      | 0 / 1          |  |  |
| Respiratory failure                             |                |  |  |
| subjects affected / exposed                     | 1 / 94 (1.06%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Psychiatric disorders                           |                |  |  |
| Mental status changes                           |                |  |  |
| subjects affected / exposed                     | 1 / 94 (1.06%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Investigations                                  |                |  |  |
| Body temperature increased                      |                |  |  |
| subjects affected / exposed                     | 1 / 94 (1.06%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Blood bilirubin increased                       |                |  |  |
| subjects affected / exposed                     | 1 / 94 (1.06%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Weight decreased                                |                |  |  |
| subjects affected / exposed                     | 1 / 94 (1.06%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Injury, poisoning and procedural complications  |                |  |  |
| Femur fracture                                  |                |  |  |
| subjects affected / exposed                     | 1 / 94 (1.06%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 1          |  |  |
| Fall  |                |  |  |
| subjects affected / exposed                     | 1 / 94 (1.06%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |

|   |                |  |  |
|---|----------------|--|--|
| Nervous system disorders                        |                |  |  |
| Cognitive disorder                              |                |  |  |
| subjects affected / exposed                     | 1 / 94 (1.06%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Coma hepatic                                    |                |  |  |
| subjects affected / exposed                     | 1 / 94 (1.06%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Headache  |                |  |  |
| subjects affected / exposed                     | 1 / 94 (1.06%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Blood and lymphatic system disorders            |                |  |  |
| Anaemia   |                |  |  |
| subjects affected / exposed                     | 4 / 94 (4.26%) |  |  |
| occurrences causally related to treatment / all | 0 / 4          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Gastrointestinal disorders                      |                |  |  |
| Abdominal pain                                  |                |  |  |
| subjects affected / exposed                     | 4 / 94 (4.26%) |  |  |
| occurrences causally related to treatment / all | 1 / 4          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Colonic fistula                                 |                |  |  |
| subjects affected / exposed                     | 1 / 94 (1.06%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Constipation                                    |                |  |  |
| subjects affected / exposed                     | 1 / 94 (1.06%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Diarrhoea                                       |                |  |  |



|   |                |  |  |  |
|---|----------------|--|--|--|
| subjects affected / exposed                     | 1 / 94 (1.06%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Gastric ulcer                                   |                |  |  |  |
| subjects affected / exposed                     | 1 / 94 (1.06%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Ileus   |                |  |  |  |
| subjects affected / exposed                     | 1 / 94 (1.06%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Immune-mediated enterocolitis                   |                |  |  |  |
| subjects affected / exposed                     | 1 / 94 (1.06%) |  |  |  |
| occurrences causally related to treatment / all | 1 / 1          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Intestinal obstruction                          |                |  |  |  |
| subjects affected / exposed                     | 2 / 94 (2.13%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 2          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Large intestinal obstruction                    |                |  |  |  |
| subjects affected / exposed                     | 1 / 94 (1.06%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Nausea  |                |  |  |  |
| subjects affected / exposed                     | 2 / 94 (2.13%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 4          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Proctalgia                                      |                |  |  |  |
| subjects affected / exposed                     | 2 / 94 (2.13%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 3          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Proctitis haemorrhagic                          |                |  |  |  |

|   |                |  |  |
|---|----------------|--|--|
| subjects affected / exposed                     | 1 / 94 (1.06%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Rectal haemorrhage                              |                |  |  |
| subjects affected / exposed                     | 1 / 94 (1.06%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Superior mesenteric artery syndrome             |                |  |  |
| subjects affected / exposed                     | 1 / 94 (1.06%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Vomiting  |                |  |  |
| subjects affected / exposed                     | 1 / 94 (1.06%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Hepatobiliary disorders                         |                |  |  |
| Cholecystitis                                   |                |  |  |
| subjects affected / exposed                     | 1 / 94 (1.06%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Cholangitis                                     |                |  |  |
| subjects affected / exposed                     | 1 / 94 (1.06%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Cholecystitis acute                             |                |  |  |
| subjects affected / exposed                     | 1 / 94 (1.06%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Hepatitis                                       |                |  |  |
| subjects affected / exposed                     | 1 / 94 (1.06%) |  |  |
| occurrences causally related to treatment / all | 1 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Skin and subcutaneous tissue disorders          |                |  |  |

|   |                |  |  |
|---|----------------|--|--|
| Purpura   |                |  |  |
| subjects affected / exposed                     | 1 / 94 (1.06%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Renal and urinary disorders                     |                |  |  |
| Acute kidney injury                             |                |  |  |
| subjects affected / exposed                     | 1 / 94 (1.06%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Haematuria                                      |                |  |  |
| subjects affected / exposed                     | 2 / 94 (2.13%) |  |  |
| occurrences causally related to treatment / all | 0 / 2          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Hydronephrosis                                  |                |  |  |
| subjects affected / exposed                     | 1 / 94 (1.06%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Ureteric compression                            |                |  |  |
| subjects affected / exposed                     | 1 / 94 (1.06%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Urinary retention                               |                |  |  |
| subjects affected / exposed                     | 1 / 94 (1.06%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Endocrine disorders                             |                |  |  |
| Adrenal insufficiency                           |                |  |  |
| subjects affected / exposed                     | 1 / 94 (1.06%) |  |  |
| occurrences causally related to treatment / all | 1 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Musculoskeletal and connective tissue disorders |                |  |  |
| Back pain                                       |                |  |  |

|   |                |  |  |
|---|----------------|--|--|
| subjects affected / exposed                     | 1 / 94 (1.06%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Bone pain                                       |                |  |  |
| subjects affected / exposed                     | 1 / 94 (1.06%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Flank pain                                      |                |  |  |
| subjects affected / exposed                     | 1 / 94 (1.06%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Infections and infestations                     |                |  |  |
| Anal abscess                                    |                |  |  |
| subjects affected / exposed                     | 1 / 94 (1.06%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Cellulitis                                      |                |  |  |
| subjects affected / exposed                     | 1 / 94 (1.06%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Device related infection                        |                |  |  |
| subjects affected / exposed                     | 1 / 94 (1.06%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Gastroenteritis                                 |                |  |  |
| subjects affected / exposed                     | 1 / 94 (1.06%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Herpes zoster                                   |                |  |  |
| subjects affected / exposed                     | 1 / 94 (1.06%) |  |  |
| occurrences causally related to treatment / all | 1 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Lyme disease                                    |                |  |  |

|   |                |  |  |  |
|---|----------------|--|--|--|
| subjects affected / exposed                     | 1 / 94 (1.06%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Pelvic infection                                |                |  |  |  |
| subjects affected / exposed                     | 1 / 94 (1.06%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |  |
| deaths causally related to treatment / all      | 0 / 1          |  |  |  |
| Pneumonia                                       |                |  |  |  |
| subjects affected / exposed                     | 2 / 94 (2.13%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 2          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Pneumocystis jirovecii pneumonia                |                |  |  |  |
| subjects affected / exposed                     | 1 / 94 (1.06%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |  |
| deaths causally related to treatment / all      | 0 / 1          |  |  |  |
| Peritonitis                                     |                |  |  |  |
| subjects affected / exposed                     | 1 / 94 (1.06%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |  |
| deaths causally related to treatment / all      | 0 / 1          |  |  |  |
| Pseudomonas infection                           |                |  |  |  |
| subjects affected / exposed                     | 1 / 94 (1.06%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Sepsis  |                |  |  |  |
| subjects affected / exposed                     | 2 / 94 (2.13%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 2          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Skin infection                                  |                |  |  |  |
| subjects affected / exposed                     | 1 / 94 (1.06%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |  |
| Stoma site infection                            |                |  |  |  |

|   |                |  |  |
|---|----------------|--|--|
| subjects affected / exposed                     | 1 / 94 (1.06%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Urinary tract infection                         |                |  |  |
| subjects affected / exposed                     | 4 / 94 (4.26%) |  |  |
| occurrences causally related to treatment / all | 0 / 4          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Metabolism and nutrition disorders              |                |  |  |
| Dehydration                                     |                |  |  |
| subjects affected / exposed                     | 1 / 94 (1.06%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Decreased appetite                              |                |  |  |
| subjects affected / exposed                     | 1 / 94 (1.06%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Hypercalcaemia                                  |                |  |  |
| subjects affected / exposed                     | 2 / 94 (2.13%) |  |  |
| occurrences causally related to treatment / all | 0 / 2          |  |  |
| deaths causally related to treatment / all      | 0 / 1          |  |  |

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

|   |                     |  |  |
|---|---------------------|--|--|
| <b>Non-serious adverse events</b>                     | Retifanlimab 500 mg |  |  |
| Total subjects affected by non-serious adverse events |                     |  |  |
| subjects affected / exposed                           | 79 / 94 (84.04%)    |  |  |
| Investigations  |                     |  |  |
| Aspartate aminotransferase increased                  |                     |  |  |
| subjects affected / exposed                           | 7 / 94 (7.45%)      |  |  |
| occurrences (all)                                     | 7                   |  |  |
| Weight decreased                                      |                     |  |  |
| subjects affected / exposed                           | 8 / 94 (8.51%)      |  |  |
| occurrences (all)                                     | 8                   |  |  |
| Nervous system disorders                              |                     |  |  |

|   |  |  |  |
|---|--|--|--|
| Headache<br>subjects affected / exposed<br>occurrences (all)  | 8 / 94 (8.51%)<br>9  |  |  |
| Blood and lymphatic system disorders<br>Anaemia<br>subjects affected / exposed<br>occurrences (all)   | 15 / 94 (15.96%)<br>19   |  |  |
| General disorders and administration site conditions<br>Asthenia<br>subjects affected / exposed<br>occurrences (all)<br><br>Fatigue<br>subjects affected / exposed<br>occurrences (all)<br><br>Pyrexia<br>subjects affected / exposed<br>occurrences (all)  | 22 / 94 (23.40%)<br>31<br><br>17 / 94 (18.09%)<br>21<br><br>10 / 94 (10.64%)<br>18   |  |  |
| Gastrointestinal disorders<br>Abdominal pain<br>subjects affected / exposed<br>occurrences (all)<br><br>Constipation<br>subjects affected / exposed<br>occurrences (all)<br><br>Diarrhoea<br>subjects affected / exposed<br>occurrences (all)<br><br>Proctalgia<br>subjects affected / exposed<br>occurrences (all)<br><br>Nausea<br>subjects affected / exposed<br>occurrences (all)<br><br>Vomiting<br>subjects affected / exposed<br>occurrences (all) | 7 / 94 (7.45%)<br>7<br><br>12 / 94 (12.77%)<br>14<br><br>20 / 94 (21.28%)<br>32<br><br>7 / 94 (7.45%)<br>7<br><br>15 / 94 (15.96%)<br>21<br><br>14 / 94 (14.89%)<br>18 |  |  |

|  |  |  |  |
|--|--|--|--|
| Rectal haemorrhage<br>subjects affected / exposed<br>occurrences (all)   | 9 / 94 (9.57%)<br>17                                 |  |  |
| Respiratory, thoracic and mediastinal disorders<br>Cough<br>subjects affected / exposed<br>occurrences (all)<br><br>Dyspnoea<br>subjects affected / exposed<br>occurrences (all)       | 11 / 94 (11.70%)<br>13<br><br>11 / 94 (11.70%)<br>13 |  |  |
| Skin and subcutaneous tissue disorders<br>Rash<br>subjects affected / exposed<br>occurrences (all)<br><br>Pruritus<br>subjects affected / exposed<br>occurrences (all)                 | 5 / 94 (5.32%)<br>6<br><br>11 / 94 (11.70%)<br>14    |  |  |
| Psychiatric disorders<br>Insomnia<br>subjects affected / exposed<br>occurrences (all)  | 6 / 94 (6.38%)<br>6                                  |  |  |
| Endocrine disorders<br>Hypothyroidism<br>subjects affected / exposed<br>occurrences (all)  | 9 / 94 (9.57%)<br>10                                 |  |  |
| Musculoskeletal and connective tissue disorders<br>Back pain<br>subjects affected / exposed<br>occurrences (all)<br><br>Arthralgia<br>subjects affected / exposed<br>occurrences (all) | 8 / 94 (8.51%)<br>9<br><br>8 / 94 (8.51%)<br>10      |  |  |
| Infections and infestations<br>Cystitis<br>subjects affected / exposed<br>occurrences (all)<br><br>Urinary tract infection   | 5 / 94 (5.32%)<br>5                                  |  |  |



|  |                     |  |  |
|--|---------------------|--|--|
| subjects affected / exposed<br>occurrences (all) | 7 / 94 (7.45%)<br>9 |  |  |
| Metabolism and nutrition disorders               |                     |  |  |
| Decreased appetite                               |                     |  |  |
| subjects affected / exposed                      | 12 / 94 (12.77%)    |  |  |
| occurrences (all)                                | 12                  |  |  |
| Hypokalaemia                                     |                     |  |  |
| subjects affected / exposed                      | 5 / 94 (5.32%)      |  |  |
| occurrences (all)                                | 5                   |  |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date            | Amendment   |
|-----------------|---|
| 06 August 2018  | The primary purpose of this amendment was to address comments regarding the design of the study.                      |
| 04 October 2018 | The purpose of this amendment was to address comments regarding the design of the study.                              |
| 21 March 2019   | The protocol was amended to add a translational substudy and to remove the requirement for premedication prophylaxis. |
| 08 July 2019    | The protocol was amended to clarify eligibility criteria.   |

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported

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### Online references

<http://www.ncbi.nlm.nih.gov/pubmed/35816951>