



## Clinical trial results:

### A Phase 2, Open-Label, Single-Agent, Multicenter Study to Evaluate the Efficacy and Safety of Pemigatinib (INCB054828) in Subjects With Metastatic or Surgically Unresectable Urothelial Carcinoma Harboring FGF/FGFR Alterations - (FIGHT-201)

#### Summary

|                          |                  |
|--------------------------|------------------|
| EudraCT number           | 2016-001321-14   |
| Trial protocol           | GB BE FR ES NL   |
| Global end of trial date | 01 February 2022 |

#### Results information

|                                |   |
|--------------------------------|---|
| Result version number          | v2 (current)  |
| This version publication date  | 09 April 2023   |
| First version publication date | 20 February 2023  |
| Version creation reason        | <ul style="list-style-type: none"><li>• Correction of full data set</li></ul> Revisions made to align with ClinicalTrials.gov record after undergoing NIH review. |

#### Trial information

##### Trial identification

|                       |                |
|-----------------------|----------------|
| Sponsor protocol code | INCB 54828-201 |
|-----------------------|----------------|

##### 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 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                       | 01 February 2022 |
| Is this the analysis of the primary completion data? | No               |
| Global end of trial reached?                         | Yes              |
| Global end of trial date                             | 01 February 2022 |
| Was the trial ended prematurely?                     | No               |

Notes:

## General information about the trial

Main objective of the trial:

The purpose of this study was to evaluate the overall response rate (ORR) of pemigatinib as a monotherapy in the treatment of metastatic or surgically unresectable urothelial carcinoma harboring fibroblast growth factor/fibroblast growth factor receptor (FGF/FGFR) alterations.

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, Good Clinical Practices as defined in Title 21 of the United States Code of Federal Regulations Parts 11, 50, 54, 56, and 312, as well as International Conference on Harmonisation Good Clinical Practice (ICH GCP) consolidated guidelines (E6), Japanese-Good Clinical Practice (J-GCP), and applicable regulatory requirements.

Background therapy: -

Evidence for comparator: -

|   |                 |
|---|-----------------|
| Actual start date of recruitment                          | 12 January 2017 |
| 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 | France: 64         |
| Country: Number of subjects enrolled | Israel: 15         |
| Country: Number of subjects enrolled | Japan: 10          |
| Country: Number of subjects enrolled | United States: 78  |
| Country: Number of subjects enrolled | Germany: 10        |
| Country: Number of subjects enrolled | Italy: 36          |
| Country: Number of subjects enrolled | Netherlands: 2     |
| Country: Number of subjects enrolled | Spain: 17          |
| Country: Number of subjects enrolled | Belgium: 14        |
| Country: Number of subjects enrolled | Denmark: 3         |
| Country: Number of subjects enrolled | United Kingdom: 11 |
| Worldwide total number of subjects   | 260                |
| EEA total number of subjects         | 146                |

Notes:

| <b>Subjects enrolled per age group</b>    |     |
|---|-----|
| In utero                                  | 0   |
| Preterm newborn - gestational age < 37 wk | 0   |
| Newborns (0-27 days)                      | 0   |
| Infants and toddlers (28 days-23 months)  | 0   |
| Children (2-11 years)                     | 0   |
| Adolescents (12-17 years)                 | 0   |
| Adults (18-64 years)                      | 91  |
| From 65 to 84 years                       | 164 |
| 85 years and over                         | 5   |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

The study was conducted at a total of 73 study centers in 11 countries (United States, France, Italy, Spain, Israel, Belgium, United Kingdom, Germany, Japan, Denmark, and the Netherlands).

### 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

|                              |   |
|------------------------------|---|
| Are arms mutually exclusive? | Yes                                     |
| <b>Arm title</b>             | Cohort A-ID: FGFR3 mutations or fusions |

Arm description:

Participants with fibroblast growth factor (FGF) receptor 3 (FGFR3) mutations or fusions self-administered oral pemigatinib at a starting dose of 13.5 milligrams (mg) once daily (QD) on an intermittent dose (ID) (2-weeks-on/1-week-off therapy) schedule in 21-day cycles. Participants who did not reach the target serum phosphate level of > 5.5 mg/deciliter (dL) could have increased the daily dose to 18 mg, provided they had no ongoing Grade 2 or higher treatment-related treatment-emergent adverse events (TEAEs), and they had been compliant with taking the study drug.

|  |              |
|--|--------------|
| Arm type                               | Experimental |
| Investigational medicinal product name | pemigatinib  |
| Investigational medicinal product code |              |
| Other name                             |              |
| Pharmaceutical forms                   | Tablet       |
| Routes of administration               | Oral use     |

Dosage and administration details:

2.0- and 4.5-mg tablets; starting dose of 13.5 mg

|                  |   |
|------------------|---|
| <b>Arm title</b> | Cohort B-ID: All other FGF/FGFR alterations |
|------------------|---|

Arm description:

Participants with all other FGF/FGFR alterations self-administered oral pemigatinib at a starting dose of 13.5 mg QD on an ID (2-weeks-on/1-week-off therapy) schedule in 21-day cycles. Participants who did not reach the target serum phosphate level of > 5.5 mg/dL could have increased the daily dose to 18 mg, provided they had no ongoing Grade 2 or higher treatment-related TEAEs, and they had been compliant with taking the study drug.

|  |              |
|--|--------------|
| Arm type                               | Experimental |
| Investigational medicinal product name | pemigatinib  |
| Investigational medicinal product code |              |
| Other name                             |              |
| Pharmaceutical forms                   | Tablet       |
| Routes of administration               | Oral use     |

Dosage and administration details:

2.0- and 4.5-mg tablets; starting dose of 13.5 mg

|                  |          |
|------------------|----------|
| <b>Arm title</b> | Other-ID |
|------------------|----------|

Arm description:

Participants with no FGF/FGFR alterations or with an undetermined FGF/FGFR status self-administered oral pemigatinib at a starting dose of 13.5 mg QD on an ID (2-weeks-on/1-week-off therapy) schedule in 21-day cycles. Participants who did not reach the target serum phosphate level of > 5.5 mg/dL could have increased the daily dose to 18 mg, provided they had no ongoing Grade 2 or higher treatment-

related TEAEs, and they had been compliant with taking the study drug.

|   |   |
|---|---|
| Arm type  | Experimental                            |
| Investigational medicinal product name            | pemigatinib                             |
| Investigational medicinal product code            |   |
| Other name  |   |
| Pharmaceutical forms                              | Tablet                                  |
| Routes of administration                          | Oral use                                |
| Dosage and administration details:                |   |
| 2.0- and 4.5-mg tablets; starting dose of 13.5 mg |   |
| <b>Arm title</b>                                  | Cohort A-CD: FGFR3 mutations or fusions |

Arm description:

Participants with FGFR3 mutations or fusions self-administered oral pemigatinib at a starting dose of 13.5 mg QD on a continuous dose (CD) (no planned dose hold) schedule in 21-day cycles. Participants who did not reach the target serum phosphate level of > 5.5 mg/dL could have increased the daily dose to 18 mg, provided they had no ongoing Grade 2 or higher treatment-related TEAEs, and they had been compliant with taking the study drug.

|   |              |
|---|--------------|
| Arm type  | Experimental |
| Investigational medicinal product name            | pemigatinib  |
| Investigational medicinal product code            |              |
| Other name  |              |
| Pharmaceutical forms                              | Tablet       |
| Routes of administration                          | Oral use     |
| Dosage and administration details:                |              |
| 2.0- and 4.5-mg tablets; starting dose of 13.5 mg |              |
| <b>Arm title</b>                                  | Other-CD     |

Arm description:

Participants with no FGF/FGFR alterations or with an undetermined FGF/FGFR status self-administered oral pemigatinib at a starting dose of 13.5 mg QD on a continuous dose (CD) (no planned dose hold) schedule in 21-day cycles. Participants who did not reach the target serum phosphate level of > 5.5 mg/dL could have increased the daily dose to 18 mg, provided they had no ongoing Grade 2 or higher treatment-related TEAEs, and they had been compliant with taking the study drug.

|  |              |
|--|--------------|
| Arm type                               | Experimental |
| Investigational medicinal product name | pemigatinib  |
| Investigational medicinal product code |              |
| Other name                             |              |
| Pharmaceutical forms                   | Tablet       |
| Routes of administration               | Oral use     |

Dosage and administration details:

2.0- and 4.5-mg tablets; starting dose of 13.5 mg

| Number of subjects in period 1 | Cohort A-ID: FGFR3 mutations or fusions | Cohort B-ID: All other FGF/FGFR alterations | Other-ID |
|--------------------------------|---|---|----------|
|                                |   |   |          |
| Started                        | 103                                     | 44  | 9        |
| Completed                      | 10                                      | 2   | 1        |
| Not completed                  | 93                                      | 42  | 8        |
| Adverse event, serious fatal   | 87                                      | 36  | 8        |
| Consent withdrawn by subject   | 1                                       | 3   | -        |
| Physician decision             | -                                       | -   | -        |

|                     |   |   |   |
|---------------------|---|---|---|
| Captured as Other   | 2 | - | - |
| Progressive Disease | 1 | 2 | - |
| Lost to follow-up   | 2 | 1 | - |

| <b>Number of subjects in period 1</b> | Cohort A-CD: FGFR3 mutations or fusions | Other-CD |
|---------------------------------------|---|----------|
| Started                               | 101                                     | 3        |
| Completed                             | 13                                      | 1        |
| Not completed                         | 88                                      | 2        |
| Adverse event, serious fatal          | 81                                      | 2        |
| Consent withdrawn by subject          | 2                                       | -        |
| Physician decision                    | 1                                       | -        |
| Captured as Other                     | 1                                       | -        |
| Progressive Disease                   | -                                       | -        |
| Lost to follow-up                     | 3                                       | -        |

## Baseline characteristics

### Reporting groups

|                       |   |
|-----------------------|---|
| Reporting group title | Cohort A-ID: FGFR3 mutations or fusions |
|-----------------------|---|

Reporting group description:

Participants with fibroblast growth factor (FGF) receptor 3 (FGFR3) mutations or fusions self-administered oral pemigatinib at a starting dose of 13.5 milligrams (mg) once daily (QD) on an intermittent dose (ID) (2-weeks-on/1-week-off therapy) schedule in 21-day cycles. Participants who did not reach the target serum phosphate level of > 5.5 mg/deciliter (dL) could have increased the daily dose to 18 mg, provided they had no ongoing Grade 2 or higher treatment-related treatment-emergent adverse events (TEAEs), and they had been compliant with taking the study drug.

|                       |   |
|-----------------------|---|
| Reporting group title | Cohort B-ID: All other FGF/FGFR alterations |
|-----------------------|---|

Reporting group description:

Participants with all other FGF/FGFR alterations self-administered oral pemigatinib at a starting dose of 13.5 mg QD on an ID (2-weeks-on/1-week-off therapy) schedule in 21-day cycles. Participants who did not reach the target serum phosphate level of > 5.5 mg/dL could have increased the daily dose to 18 mg, provided they had no ongoing Grade 2 or higher treatment-related TEAEs, and they had been compliant with taking the study drug.

|                       |          |
|-----------------------|----------|
| Reporting group title | Other-ID |
|-----------------------|----------|

Reporting group description:

Participants with no FGF/FGFR alterations or with an undetermined FGF/FGFR status self-administered oral pemigatinib at a starting dose of 13.5 mg QD on an ID (2-weeks-on/1-week-off therapy) schedule in 21-day cycles. Participants who did not reach the target serum phosphate level of > 5.5 mg/dL could have increased the daily dose to 18 mg, provided they had no ongoing Grade 2 or higher treatment-related TEAEs, and they had been compliant with taking the study drug.

|                       |   |
|-----------------------|---|
| Reporting group title | Cohort A-CD: FGFR3 mutations or fusions |
|-----------------------|---|

Reporting group description:

Participants with FGFR3 mutations or fusions self-administered oral pemigatinib at a starting dose of 13.5 mg QD on a continuous dose (CD) (no planned dose hold) schedule in 21-day cycles. Participants who did not reach the target serum phosphate level of > 5.5 mg/dL could have increased the daily dose to 18 mg, provided they had no ongoing Grade 2 or higher treatment-related TEAEs, and they had been compliant with taking the study drug.

|                       |          |
|-----------------------|----------|
| Reporting group title | Other-CD |
|-----------------------|----------|

Reporting group description:

Participants with no FGF/FGFR alterations or with an undetermined FGF/FGFR status self-administered oral pemigatinib at a starting dose of 13.5 mg QD on a continuous dose (CD) (no planned dose hold) schedule in 21-day cycles. Participants who did not reach the target serum phosphate level of > 5.5 mg/dL could have increased the daily dose to 18 mg, provided they had no ongoing Grade 2 or higher treatment-related TEAEs, and they had been compliant with taking the study drug.

| Reporting group values                   | Cohort A-ID: FGFR3 mutations or fusions | Cohort B-ID: All other FGF/FGFR alterations | Other-ID |
|--|---|---|----------|
| Number of subjects                       | 103                                     | 44  | 9        |
| Age categorical<br>Units: Subjects       |   |   |          |
| Adults (18-64 years)                     | 40                                      | 19  | 3        |
| From 65-84 years                         | 60                                      | 25  | 6        |
| 85 years and over                        | 3                                       | 0   | 0        |
| Age Continuous<br>Units: years           |   |   |          |
| arithmetic mean                          | 67.6                                    | 65.1  | 69.3     |
| standard deviation                       | ± 9.09                                  | ± 10.83                                     | ± 7.98   |
| Sex: Female, Male<br>Units: participants |   |   |          |
| Female                                   | 29                                      | 14  | 1        |

|      |    |    |   |
|------|----|----|---|
| Male | 74 | 30 | 8 |
|------|----|----|---|

|  |    |    |   |
|--|----|----|---|
| Race, Customized<br>Units: Subjects      |    |    |   |
| White                                    | 64 | 29 | 6 |
| Black or African-American                | 0  | 0  | 1 |
| Asian                                    | 2  | 2  | 0 |
| Turkish                                  | 1  | 0  | 0 |
| Persian                                  | 0  | 0  | 1 |
| Unknown or Not Reported                  | 30 | 13 | 1 |
| Missing                                  | 6  | 0  | 0 |
| Ethnicity, Customized<br>Units: Subjects |    |    |   |
| Hispanic or Latino                       | 1  | 0  | 0 |
| Not Hispanic or Latino                   | 64 | 32 | 7 |
| Not Reported                             | 23 | 11 | 2 |
| Unknown                                  | 5  | 1  | 0 |
| Captured as Other                        | 5  | 0  | 0 |
| Missing                                  | 5  | 0  | 0 |

| Reporting group values                   | Cohort A-CD: FGFR3 mutations or fusions | Other-CD | Total |
|--|---|----------|-------|
| Number of subjects                       | 101                                     | 3        | 260   |
| Age categorical<br>Units: Subjects       |   |          |       |
| Adults (18-64 years)                     | 27                                      | 2        | 91    |
| From 65-84 years                         | 72                                      | 1        | 164   |
| 85 years and over                        | 2                                       | 0        | 5     |
| Age Continuous<br>Units: years           |   |          |       |
| arithmetic mean                          | 68.5                                    | 60.3     |       |
| standard deviation                       | ± 9.39                                  | ± 9.02   | -     |
| Sex: Female, Male<br>Units: participants |   |          |       |
| Female                                   | 23                                      | 1        | 68    |
| Male                                     | 78                                      | 2        | 192   |
| Race, Customized<br>Units: Subjects      |   |          |       |
| White                                    | 63                                      | 2        | 164   |
| Black or African-American                | 0                                       | 0        | 1     |
| Asian                                    | 12                                      | 1        | 17    |
| Turkish                                  | 0                                       | 0        | 1     |
| Persian                                  | 0                                       | 0        | 1     |
| Unknown or Not Reported                  | 22                                      | 0        | 66    |
| Missing                                  | 4                                       | 0        | 10    |
| Ethnicity, Customized<br>Units: Subjects |   |          |       |
| Hispanic or Latino                       | 2                                       | 0        | 3     |
| Not Hispanic or Latino                   | 66                                      | 2        | 171   |
| Not Reported                             | 22                                      | 1        | 59    |
| Unknown                                  | 3                                       | 0        | 9     |



|                   |   |   |    |
|-------------------|---|---|----|
| Captured as Other | 6 | 0 | 11 |
| Missing           | 2 | 0 | 7  |

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## End points

### End points reporting groups

|   |   |
|---|---|
| Reporting group title   | Cohort A-ID: FGFR3 mutations or fusions     |
| Reporting group description:<br>Participants with fibroblast growth factor (FGF) receptor 3 (FGFR3) mutations or fusions self-administered oral pemigatinib at a starting dose of 13.5 milligrams (mg) once daily (QD) on an intermittent dose (ID) (2-weeks-on/1-week-off therapy) schedule in 21-day cycles. Participants who did not reach the target serum phosphate level of > 5.5 mg/deciliter (dL) could have increased the daily dose to 18 mg, provided they had no ongoing Grade 2 or higher treatment-related treatment-emergent adverse events (TEAEs), and they had been compliant with taking the study drug. |   |
| Reporting group title   | Cohort B-ID: All other FGF/FGFR alterations |
| Reporting group description:<br>Participants with all other FGF/FGFR alterations self-administered oral pemigatinib at a starting dose of 13.5 mg QD on an ID (2-weeks-on/1-week-off therapy) schedule in 21-day cycles. Participants who did not reach the target serum phosphate level of > 5.5 mg/dL could have increased the daily dose to 18 mg, provided they had no ongoing Grade 2 or higher treatment-related TEAEs, and they had been compliant with taking the study drug.   |   |
| Reporting group title   | Other-ID                                    |
| Reporting group description:<br>Participants with no FGF/FGFR alterations or with an undetermined FGF/FGFR status self-administered oral pemigatinib at a starting dose of 13.5 mg QD on an ID (2-weeks-on/1-week-off therapy) schedule in 21-day cycles. Participants who did not reach the target serum phosphate level of > 5.5 mg/dL could have increased the daily dose to 18 mg, provided they had no ongoing Grade 2 or higher treatment-related TEAEs, and they had been compliant with taking the study drug.  |   |
| Reporting group title   | Cohort A-CD: FGFR3 mutations or fusions     |
| Reporting group description:<br>Participants with FGFR3 mutations or fusions self-administered oral pemigatinib at a starting dose of 13.5 mg QD on a continuous dose (CD) (no planned dose hold) schedule in 21-day cycles. Participants who did not reach the target serum phosphate level of > 5.5 mg/dL could have increased the daily dose to 18 mg, provided they had no ongoing Grade 2 or higher treatment-related TEAEs, and they had been compliant with taking the study drug.   |   |
| Reporting group title   | Other-CD                                    |
| Reporting group description:<br>Participants with no FGF/FGFR alterations or with an undetermined FGF/FGFR status self-administered oral pemigatinib at a starting dose of 13.5 mg QD on a continuous dose (CD) (no planned dose hold) schedule in 21-day cycles. Participants who did not reach the target serum phosphate level of > 5.5 mg/dL could have increased the daily dose to 18 mg, provided they had no ongoing Grade 2 or higher treatment-related TEAEs, and they had been compliant with taking the study drug.  |   |
| Subject analysis set title  | Cohort A-ID + Cohort B-ID                   |
| Subject analysis set type   | Full analysis                               |
| Subject analysis set description:<br>Participants with FGFR3 mutations or fusions (Cohort A) or with all other FGF/FGFR alterations (Cohort B) self-administered oral pemigatinib at a starting dose of 13.5 mg QD on an ID (2-weeks-on/1-week-off therapy) schedule in 21-day cycles. Participants who did not reach the target serum phosphate level of > 5.5 mg/dL could have increased the daily dose to 18 mg, provided they had no ongoing Grade 2 or higher treatment-related TEAEs, and they had been compliant with taking the study drug.   |   |
| Subject analysis set title  | Cohort A-ID + Cohort A-CD                   |
| Subject analysis set type   | Full analysis                               |
| Subject analysis set description:<br>Participants with FGFR3 mutations or fusions self-administered oral pemigatinib at a starting dose of 13.5 mg QD on an ID (2-weeks-on/1-week-off therapy) schedule (Cohort A-ID) or on a CD (no planned dose hold) schedule (Cohort A-CD) in 21-day cycles. Participants who did not reach the target serum phosphate level of > 5.5 mg/dL could have increased the daily dose to 18 mg, provided they had no ongoing Grade 2 or higher treatment-related TEAEs, and they had been compliant with taking the study drug.   |   |
| Subject analysis set title  | Cohort A-ID + Cohort B-ID + Cohort A-CD     |
| Subject analysis set type   | Full analysis                               |

Subject analysis set description:

Participants with FGFR3 mutations or fusions (Cohort A) or with all other FGF/FGFR alterations (Cohort B) self-administered oral pemigatinib at a starting dose of 13.5 mg QD on an ID (2-weeks-on/1-week-off therapy) schedule (Cohort A-ID and Cohort B-ID) in 21-day cycles or on a CD (no planned dose hold) schedule (Cohort A-CD). Participants who did not reach the target serum phosphate level of > 5.5 mg/dL could have increased the daily dose to 18 mg, provided they had no ongoing Grade 2 or higher treatment-related TEAEs, and they had been compliant with taking the study drug.

### Primary: Objective Response Rate (ORR) in participants with FGFR3 mutations or fusions on a CD regimen

|                 |  |
|-----------------|--|
| End point title | Objective Response Rate (ORR) in participants with FGFR3 mutations or fusions on a CD regimen <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) at any post-Baseline visit prior to first progressive disease (PD), per Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1 (v1.1). 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. FGF/FGF status was based on central genomics laboratory results. Response was based on review of scans by an independent centralized radiological review committee. Response was confirmed.

|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

up to 1138 days

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                  | Cohort A-ID:<br>FGFR3<br>mutations or<br>fusions | Cohort B-ID:<br>All other<br>FGF/FGFR<br>alterations | Other-ID         | Cohort A-CD:<br>FGFR3<br>mutations or<br>fusions |
|-----------------------------------|--|--|------------------|--|
| Subject group type                | Reporting group                                  | Reporting group                                      | Reporting group  | Reporting group                                  |
| Number of subjects analysed       | 0 <sup>[2]</sup>                                 | 0 <sup>[3]</sup>                                     | 0 <sup>[4]</sup> | 101  |
| Units: percentage of participants |  |  |                  |  |
| number (confidence interval 95%)  | ( to )   | ( to )   | ( to )           | 17.8 (10.92 to 26.70)                            |

Notes:

[2] - Analysis was conducted in participants with FGFR3 mutations or fusions on a CD regimen.

[3] - Analysis was conducted in participants with FGFR3 mutations or fusions on a CD regimen.

[4] - Analysis was conducted in participants with FGFR3 mutations or fusions on a CD regimen.

| End point values                  | Other-CD         |  |  |  |
|-----------------------------------|------------------|--|--|--|
| Subject group type                | Reporting group  |  |  |  |
| Number of subjects analysed       | 0 <sup>[5]</sup> |  |  |  |
| Units: percentage of participants |                  |  |  |  |
| number (confidence interval 95%)  | ( to )           |  |  |  |

Notes:

[5] - Analysis was conducted in participants with FGFR3 mutations or fusions on a CD regimen.

### Statistical analyses

No statistical analyses for this end point

**Secondary: ORR in participants with FGFR3 mutations or fusions on an ID regimen**

|                 |  |
|-----------------|--|
| End point title | ORR in participants with FGFR3 mutations or fusions on an ID regimen |
|-----------------|--|

## End point description:

ORR was defined as the percentage of participants with a best overall response of CR or PR at any post-Baseline visit prior to first PD, per RECIST v1.1. 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. FGFR/FGF status was based on central genomics laboratory results. Response was based on review of scans by an independent centralized radiological review committee. Response was confirmed.

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

## End point timeframe:

up to 817 days

| End point values                  | Cohort A-ID: FGFR3 mutations or fusions | Cohort B-ID: All other FGF/FGFR alterations | Other-ID         | Cohort A-CD: FGFR3 mutations or fusions |
|-----------------------------------|---|---|------------------|---|
| Subject group type                | Reporting group                         | Reporting group                             | Reporting group  | Reporting group                         |
| Number of subjects analysed       | 103                                     | 0 <sup>[6]</sup>                            | 0 <sup>[7]</sup> | 0 <sup>[8]</sup>                        |
| Units: percentage of participants |   |   |                  |   |
| number (confidence interval 95%)  | 23.3 (15.54 to 32.66)                   | ( to )                                      | ( to )           | ( to )                                  |

## Notes:

[6] - Analysis was conducted in participants with FGFR3 mutations or fusions on an ID regimen.

[7] - Analysis was conducted in participants with FGFR3 mutations or fusions on an ID regimen.

[8] - Analysis was conducted in participants with FGFR3 mutations or fusions on an ID regimen.

| End point values                  | Other-CD         |  |  |  |
|-----------------------------------|------------------|--|--|--|
| Subject group type                | Reporting group  |  |  |  |
| Number of subjects analysed       | 0 <sup>[9]</sup> |  |  |  |
| Units: percentage of participants |                  |  |  |  |
| number (confidence interval 95%)  | ( to )           |  |  |  |

## Notes:

[9] - Analysis was conducted in participants with FGFR3 mutations or fusions on an ID regimen.

**Statistical analyses**

No statistical analyses for this end point

**Secondary: ORR in participants with all other FGF/FGFR alterations**

|                 |   |
|-----------------|---|
| End point title | ORR in participants with all other FGF/FGFR alterations |
|-----------------|---|

## End point description:

ORR was defined as the percentage of participants with a best overall response of CR or PR at any post-Baseline visit prior to first PD, per RECIST v1.1. 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. FGFR/FGF status was based on central genomics laboratory results. Response was based on review of scans by an independent centralized radiological review committee. Response was confirmed.

|   |           |
|---|-----------|
| End point type                          | Secondary |
| End point timeframe:<br>up to 1198 days |           |

| End point values                  | Cohort A-ID:<br>FGFR3<br>mutations or<br>fusions | Cohort B-ID:<br>All other<br>FGF/FGFR<br>alterations | Other-ID          | Cohort A-CD:<br>FGFR3<br>mutations or<br>fusions |
|-----------------------------------|--|--|-------------------|--|
| Subject group type                | Reporting group                                  | Reporting group                                      | Reporting group   | Reporting group                                  |
| Number of subjects analysed       | 0 <sup>[10]</sup>                                | 44   | 0 <sup>[11]</sup> | 0 <sup>[12]</sup>                                |
| Units: percentage of participants |  |  |                   |  |
| number (confidence interval 95%)  | ( to )   | 6.8 (1.43 to 18.66)                                  | ( to )            | ( to )   |

Notes:

[10] - Analysis was conducted in participants with all other FGF/FGFR alterations.

[11] - Analysis was conducted in participants with all other FGF/FGFR alterations.

[12] - Analysis was conducted in participants with all other FGF/FGFR alterations.

| End point values                  | Other-CD          |  |  |  |
|-----------------------------------|-------------------|--|--|--|
| Subject group type                | Reporting group   |  |  |  |
| Number of subjects analysed       | 0 <sup>[13]</sup> |  |  |  |
| Units: percentage of participants |                   |  |  |  |
| number (confidence interval 95%)  | ( to )            |  |  |  |

Notes:

[13] - Analysis was conducted in participants with all other FGF/FGFR alterations.

## Statistical analyses

No statistical analyses for this end point

## Secondary: ORR in all participants on an ID or CD regimen in combined cohorts

|                 |  |
|-----------------|--|
| End point title | ORR in all participants on an ID or CD regimen in combined cohorts |
|-----------------|--|

End point description:

ORR was defined as the percentage of participants with a best overall response of CR or PR at any post-Baseline visit prior to first PD, per RECIST v1.1. 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. FGFR/FGF status was based on central genomics laboratory results. Response was based on review of scans by an independent centralized radiological review committee. Response was confirmed.

|   |           |
|---|-----------|
| End point type                          | Secondary |
| End point timeframe:<br>up to 1198 days |           |

| End point values                  | Cohort A-ID: FGFR3 mutations or fusions | Cohort B-ID: All other FGF/FGFR alterations | Other-ID          | Cohort A-CD: FGFR3 mutations or fusions |
|-----------------------------------|---|---|-------------------|---|
| Subject group type                | Reporting group                         | Reporting group                             | Reporting group   | Reporting group                         |
| Number of subjects analysed       | 0 <sup>[14]</sup>                       | 0 <sup>[15]</sup>                           | 0 <sup>[16]</sup> | 0 <sup>[17]</sup>                       |
| Units: percentage of participants |   |   |                   |   |
| number (confidence interval 95%)  | ( to )                                  | ( to )                                      | ( to )            | ( to )                                  |

Notes:

[14] - Analysis was conducted in participants on an ID or CD regimen in combined cohorts.

[15] - Analysis was conducted in participants on an ID or CD regimen in combined cohorts.

[16] - Analysis was conducted in participants on an ID or CD regimen in combined cohorts.

[17] - Analysis was conducted in participants on an ID or CD regimen in combined cohorts.

| End point values                  | Other-CD          | Cohort A-ID + Cohort B-ID | Cohort A-ID + Cohort A-CD | Cohort A-ID + Cohort B-ID + Cohort A-CD |
|-----------------------------------|-------------------|---------------------------|---------------------------|---|
| Subject group type                | Reporting group   | Subject analysis set      | Subject analysis set      | Subject analysis set                    |
| Number of subjects analysed       | 0 <sup>[18]</sup> | 147                       | 204                       | 248                                     |
| Units: percentage of participants |                   |                           |                           |   |
| number (confidence interval 95%)  | ( to )            | 18.4 (12.47 to 25.59)     | 20.6 (15.26 to 26.79)     | 18.1 (13.55 to 23.52)                   |

Notes:

[18] - Analysis was conducted in participants on an ID or CD regimen in combined cohorts.

## 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) was defined as any untoward medical occurrence associated with the use of a drug in humans, whether or not considered drug related, that occurred after a participant provided informed consent. Abnormal laboratory values or test results occurring after informed consent constituted AEs only if they induced clinical signs or symptoms, were considered clinically meaningful, required therapy (e.g., hematologic abnormality that required transfusion), or required changes in the study drug(s). A TEAE was any AE either reported for the first time or the worsening of a pre-existing event after the first dose of study drug and within 30 days of the last dose of study drug.

|                      |                              |
|----------------------|------------------------------|
| End point type       | Secondary                    |
| End point timeframe: | up to approximately 25 weeks |

| End point values            | Cohort A-ID: FGFR3 mutations or fusions | Cohort B-ID: All other FGF/FGFR alterations | Other-ID        | Cohort A-CD: FGFR3 mutations or fusions |
|-----------------------------|---|---|-----------------|---|
| Subject group type          | Reporting group                         | Reporting group                             | Reporting group | Reporting group                         |
| Number of subjects analysed | 103                                     | 44  | 9               | 101                                     |
| Units: participants         | 103                                     | 44  | 9               | 100                                     |

|                             |                 |  |  |  |
|-----------------------------|-----------------|--|--|--|
| <b>End point values</b>     | Other-CD        |  |  |  |
| Subject group type          | Reporting group |  |  |  |
| Number of subjects analysed | 3               |  |  |  |
| Units: participants         | 3               |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Progression-free Survival (PFS)

|   |                                 |
|---|---------------------------------|
| End point title   | Progression-free Survival (PFS) |
| End point description:  |                                 |
| PFS was defined as the length of time from the start of the study drug (Day 1) to the earlier of death or disease progression by RECIST v1.1, as assessed by the independent centralized radiological review committee. |                                 |
| End point type  | Secondary                       |
| End point timeframe:  |                                 |
| up to 1138 days   |                                 |

| End point values                 | Cohort A-ID:<br>FGFR3<br>mutations or<br>fusions | Cohort B-ID:<br>All other<br>FGF/FGFR<br>alterations | Other-ID          | Cohort A-CD:<br>FGFR3<br>mutations or<br>fusions |
|----------------------------------|--|--|-------------------|--|
| Subject group type               | Reporting group                                  | Reporting group                                      | Reporting group   | Reporting group                                  |
| Number of subjects analysed      | 103  | 44   | 0 <sup>[19]</sup> | 101  |
| Units: months                    |  |  |                   |  |
| median (confidence interval 95%) | 4.27 (3.91 to 6.05)                              | 2.04 (1.87 to 2.17)                                  | ( to )            | 4.04 (3.45 to 4.17)                              |

Notes:

[19] - The "Other-ID" treatment group was not included in the Efficacy Evaluable Population.

|                                  |                   |  |  |  |
|----------------------------------|-------------------|--|--|--|
| <b>End point values</b>          | Other-CD          |  |  |  |
| Subject group type               | Reporting group   |  |  |  |
| Number of subjects analysed      | 0 <sup>[20]</sup> |  |  |  |
| Units: months                    |                   |  |  |  |
| median (confidence interval 95%) | ( to )            |  |  |  |

Notes:

[20] - The "Other-CD" treatment group was not included in the Efficacy Evaluable Population.

## 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 the first overall response contributing to an objective response (CR or PR) to the earlier of death or first overall response of PD occurring after the first overall response contributing to the objective response. 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. 9999 = The upper limit of the confidence interval was not estimable because too few participants had disease progression or died. Only participants with a CR or PR were analyzed. Response was based on review of scans by an independent centralized radiological review committee. Response was confirmed.

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

End point timeframe:

up to 1075 days

| End point values                 | Cohort A-ID:<br>FGFR3<br>mutations or<br>fusions | Cohort B-ID:<br>All other<br>FGF/FGFR<br>alterations | Other-ID          | Cohort A-CD:<br>FGFR3<br>mutations or<br>fusions |
|----------------------------------|--|--|-------------------|--|
| Subject group type               | Reporting group                                  | Reporting group                                      | Reporting group   | Reporting group                                  |
| Number of subjects analysed      | 24   | 3  | 0 <sup>[21]</sup> | 18   |
| Units: months                    |  |  |                   |  |
| median (confidence interval 95%) | 6.21 (4.60 to 7.95)                              | 10.02 (8.38 to 9999)                                 | ( to )            | 6.23 (4.14 to 8.25)                              |

Notes:

[21] - The "Other-ID" treatment group was not included in the Efficacy Evaluable Population.

| End point values                 | Other-CD          |  |  |  |
|----------------------------------|-------------------|--|--|--|
| Subject group type               | Reporting group   |  |  |  |
| Number of subjects analysed      | 0 <sup>[22]</sup> |  |  |  |
| Units: months                    |                   |  |  |  |
| median (confidence interval 95%) | ( to )            |  |  |  |

Notes:

[22] - The "Other-CD" treatment group was not included in the Efficacy 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 length of time from the start of the study drug (Day 1) until the date of death due to any cause.

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

End point timeframe:

up to 1610 days



| <b>End point values</b>          | Cohort A-ID:<br>FGFR3<br>mutations or<br>fusions | Cohort B-ID:<br>All other<br>FGF/FGFR<br>alterations | Other-ID          | Cohort A-CD:<br>FGFR3<br>mutations or<br>fusions |
|----------------------------------|--|--|-------------------|--|
| Subject group type               | Reporting group                                  | Reporting group                                      | Reporting group   | Reporting group                                  |
| Number of subjects analysed      | 103  | 44   | 0 <sup>[23]</sup> | 101  |
| Units: months                    |  |  |                   |  |
| median (confidence interval 95%) | 8.90 (7.46 to<br>15.18)                          | 9.13 (5.52 to<br>17.05)                              | ( to )            | 6.80 (5.26 to<br>9.10)                           |

Notes:

[23] - The "Other-ID" treatment group was not included in the Efficacy Evaluable Population.

| <b>End point values</b>          | Other-CD          |  |  |  |
|----------------------------------|-------------------|--|--|--|
| Subject group type               | Reporting group   |  |  |  |
| Number of subjects analysed      | 0 <sup>[24]</sup> |  |  |  |
| Units: months                    |                   |  |  |  |
| median (confidence interval 95%) | ( to )            |  |  |  |

Notes:

[24] - The "Other-CD" treatment group was not included in the Efficacy Evaluable Population.

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Adverse events were assessed for up to approximately 25 weeks; All-cause Mortality was assessed for up to 1610 days.

Adverse event reporting additional description:

Treatment-emergent adverse events, defined as adverse events either reported for the first time or the worsening of pre-existing events after the first dose of study drug and within 30 days of the last dose of study drug, have been reported.

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

### Dictionary used

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

|                    |    |
|--------------------|----|
| Dictionary version | 24 |
|--------------------|----|

### Reporting groups

|                       |   |
|-----------------------|---|
| Reporting group title | Cohort A-ID: FGFR3 mutations or fusions |
|-----------------------|---|

Reporting group description:

Participants with fibroblast growth factor (FGF) receptor 3 (FGFR3) mutations or fusions self-administered oral pemigatinib at a starting dose of 13.5 milligrams (mg) once daily (QD) on an intermittent dose (ID) (2-weeks-on/1-week-off therapy) schedule in 21-day cycles. Participants who did not reach the target serum phosphate level of > 5.5 mg/deciliter (dL) could have increased the daily dose to 18 mg, provided they had no ongoing Grade 2 or higher treatment-related treatment-emergent adverse events (TEAEs), and they had been compliant with taking the study drug.

|                       |   |
|-----------------------|---|
| Reporting group title | Cohort B-ID: All other FGF/FGFR alterations |
|-----------------------|---|

Reporting group description:

Participants with all other FGF/FGFR alterations self-administered oral pemigatinib at a starting dose of 13.5 mg QD on an ID (2-weeks-on/1-week-off therapy) schedule in 21-day cycles. Participants who did not reach the target serum phosphate level of > 5.5 mg/dL could have increased the daily dose to 18 mg, provided they had no ongoing Grade 2 or higher treatment-related TEAEs, and they had been compliant with taking the study drug.

|                       |          |
|-----------------------|----------|
| Reporting group title | Other-ID |
|-----------------------|----------|

Reporting group description:

Participants with no FGF/FGFR alterations or with an undetermined FGF/FGFR status self-administered oral pemigatinib at a starting dose of 13.5 mg QD on an ID (2-weeks-on/1-week-off therapy) schedule in 21-day cycles. Participants who did not reach the target serum phosphate level of > 5.5 mg/dL could have increased the daily dose to 18 mg, provided they had no ongoing Grade 2 or higher treatment-related TEAEs, and they had been compliant with taking the study drug.

|                       |   |
|-----------------------|---|
| Reporting group title | Cohort A-CD: FGFR3 mutations or fusions |
|-----------------------|---|

Reporting group description:

Participants with FGFR3 mutations or fusions self-administered oral pemigatinib at a starting dose of 13.5 mg QD on a continuous dose (CD) (no planned dose hold) schedule in 21-day cycles. Participants who did not reach the target serum phosphate level of > 5.5 mg/dL could have increased the daily dose to 18 mg, provided they had no ongoing Grade 2 or higher treatment-related TEAEs, and they had been compliant with taking the study drug.

|                       |          |
|-----------------------|----------|
| Reporting group title | Other-CD |
|-----------------------|----------|

Reporting group description:

Participants with no FGF/FGFR alterations or with an undetermined FGF/FGFR status self-administered oral pemigatinib at a starting dose of 13.5 mg QD on a continuous dose (CD) (no planned dose hold) schedule in 21-day cycles. Participants who did not reach the target serum phosphate level of > 5.5 mg/dL could have increased the daily dose to 18 mg, provided they had no ongoing Grade 2 or higher treatment-related TEAEs, and they had been compliant with taking the study drug.

| Serious adverse events  | Cohort A-ID: FGFR3 mutations or fusions | Cohort B-ID: All other FGF/FGFR alterations | Other-ID       |
|---|---|---|----------------|
| Total subjects affected by serious adverse events                   |   |   |                |
| subjects affected / exposed   | 45 / 103 (43.69%)                       | 26 / 44 (59.09%)                            | 3 / 9 (33.33%) |
| number of deaths (all causes)                                       | 88                                      | 39  | 8              |
| number of deaths resulting from adverse events                      | 14                                      | 6   | 0              |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |   |   |                |
| Cancer pain   |   |   |                |
| subjects affected / exposed   | 1 / 103 (0.97%)                         | 0 / 44 (0.00%)                              | 0 / 9 (0.00%)  |
| occurrences causally related to treatment / all                     | 0 / 1                                   | 0 / 0                                       | 0 / 0          |
| deaths causally related to treatment / all                          | 0 / 0                                   | 0 / 0                                       | 0 / 0          |
| Lung adenocarcinoma   |   |   |                |
| subjects affected / exposed   | 1 / 103 (0.97%)                         | 0 / 44 (0.00%)                              | 0 / 9 (0.00%)  |
| occurrences causally related to treatment / all                     | 0 / 1                                   | 0 / 0                                       | 0 / 0          |
| deaths causally related to treatment / all                          | 0 / 0                                   | 0 / 0                                       | 0 / 0          |
| Malignant neoplasm progression                                      |   |   |                |
| subjects affected / exposed   | 0 / 103 (0.00%)                         | 1 / 44 (2.27%)                              | 0 / 9 (0.00%)  |
| occurrences causally related to treatment / all                     | 0 / 0                                   | 0 / 1                                       | 0 / 0          |
| deaths causally related to treatment / all                          | 0 / 0                                   | 0 / 1                                       | 0 / 0          |
| Rectal cancer   |   |   |                |
| subjects affected / exposed   | 0 / 103 (0.00%)                         | 0 / 44 (0.00%)                              | 0 / 9 (0.00%)  |
| occurrences causally related to treatment / all                     | 0 / 0                                   | 0 / 0                                       | 0 / 0          |
| deaths causally related to treatment / all                          | 0 / 0                                   | 0 / 0                                       | 0 / 0          |
| Tumour associated fever   |   |   |                |
| subjects affected / exposed   | 0 / 103 (0.00%)                         | 0 / 44 (0.00%)                              | 0 / 9 (0.00%)  |
| occurrences causally related to treatment / all                     | 0 / 0                                   | 0 / 0                                       | 0 / 0          |
| deaths causally related to treatment / all                          | 0 / 0                                   | 0 / 0                                       | 0 / 0          |
| Tumour pain   |   |   |                |
| subjects affected / exposed   | 0 / 103 (0.00%)                         | 0 / 44 (0.00%)                              | 0 / 9 (0.00%)  |
| occurrences causally related to treatment / all                     | 0 / 0                                   | 0 / 0                                       | 0 / 0          |
| deaths causally related to treatment / all                          | 0 / 0                                   | 0 / 0                                       | 0 / 0          |
| Vascular disorders  |   |   |                |
| Hypertension  |   |   |                |

|  |                 |                |               |
|--|-----------------|----------------|---------------|
| subjects affected / exposed                          | 1 / 103 (0.97%) | 0 / 44 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 1           | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0          | 0 / 0         |
| Hypotension  |                 |                |               |
| subjects affected / exposed                          | 0 / 103 (0.00%) | 1 / 44 (2.27%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 1          | 0 / 0         |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0          | 0 / 0         |
| Hypovolaemic shock                                   |                 |                |               |
| subjects affected / exposed                          | 0 / 103 (0.00%) | 0 / 44 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0          | 0 / 0         |
| Phlebitis  |                 |                |               |
| subjects affected / exposed                          | 1 / 103 (0.97%) | 0 / 44 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all      | 1 / 1           | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0          | 0 / 0         |
| Vasculitis necrotising                               |                 |                |               |
| subjects affected / exposed                          | 0 / 103 (0.00%) | 1 / 44 (2.27%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 2          | 0 / 0         |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0          | 0 / 0         |
| Venous thrombosis                                    |                 |                |               |
| subjects affected / exposed                          | 1 / 103 (0.97%) | 0 / 44 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 1           | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0          | 0 / 0         |
| General disorders and administration site conditions |                 |                |               |
| Asthenia   |                 |                |               |
| subjects affected / exposed                          | 0 / 103 (0.00%) | 0 / 44 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0          | 0 / 0         |
| Catheter site inflammation                           |                 |                |               |
| subjects affected / exposed                          | 0 / 103 (0.00%) | 0 / 44 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0          | 0 / 0         |
| Disease progression                                  |                 |                |               |

|   |                 |                |                |
|---|-----------------|----------------|----------------|
| subjects affected / exposed                     | 2 / 103 (1.94%) | 0 / 44 (0.00%) | 0 / 9 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 2           | 0 / 0          | 0 / 0          |
| <b>Fatigue</b>                                  |                 |                |                |
| subjects affected / exposed                     | 1 / 103 (0.97%) | 1 / 44 (2.27%) | 0 / 9 (0.00%)  |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0          |
| <b>Gait disturbance</b>                         |                 |                |                |
| subjects affected / exposed                     | 0 / 103 (0.00%) | 1 / 44 (2.27%) | 0 / 9 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0          |
| <b>General physical health deterioration</b>    |                 |                |                |
| subjects affected / exposed                     | 5 / 103 (4.85%) | 3 / 44 (6.82%) | 0 / 9 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 5           | 0 / 3          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 5           | 0 / 3          | 0 / 0          |
| <b>Malaise</b>                                  |                 |                |                |
| subjects affected / exposed                     | 0 / 103 (0.00%) | 1 / 44 (2.27%) | 0 / 9 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0           | 1 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0          |
| <b>Pain</b>                                     |                 |                |                |
| subjects affected / exposed                     | 0 / 103 (0.00%) | 2 / 44 (4.55%) | 0 / 9 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 2          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0          |
| <b>Polyp</b>                                    |                 |                |                |
| subjects affected / exposed                     | 1 / 103 (0.97%) | 0 / 44 (0.00%) | 0 / 9 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0          |
| <b>Pyrexia</b>                                  |                 |                |                |
| subjects affected / exposed                     | 1 / 103 (0.97%) | 1 / 44 (2.27%) | 1 / 9 (11.11%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0          |
| <b>Sudden death</b>                             |                 |                |                |

|   |                 |                |                |
|---|-----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 103 (0.00%) | 0 / 44 (0.00%) | 0 / 9 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0          |
| Systemic inflammatory response syndrome         |                 |                |                |
| subjects affected / exposed                     | 1 / 103 (0.97%) | 0 / 44 (0.00%) | 0 / 9 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0          |
| Immune system disorders                         |                 |                |                |
| Anaphylactic shock                              |                 |                |                |
| subjects affected / exposed                     | 0 / 103 (0.00%) | 0 / 44 (0.00%) | 0 / 9 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0          |
| Respiratory, thoracic and mediastinal disorders |                 |                |                |
| Cough   |                 |                |                |
| subjects affected / exposed                     | 0 / 103 (0.00%) | 0 / 44 (0.00%) | 1 / 9 (11.11%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0          |
| Dyspnoea  |                 |                |                |
| subjects affected / exposed                     | 2 / 103 (1.94%) | 0 / 44 (0.00%) | 0 / 9 (0.00%)  |
| occurrences causally related to treatment / all | 1 / 2           | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 1           | 0 / 0          | 0 / 0          |
| Dyspnoea exertional                             |                 |                |                |
| subjects affected / exposed                     | 1 / 103 (0.97%) | 0 / 44 (0.00%) | 0 / 9 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0          |
| Hiccups   |                 |                |                |
| subjects affected / exposed                     | 0 / 103 (0.00%) | 1 / 44 (2.27%) | 0 / 9 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0          |
| Hypoxia   |                 |                |                |
| subjects affected / exposed                     | 1 / 103 (0.97%) | 0 / 44 (0.00%) | 0 / 9 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0          |

|   |                 |                |               |
|---|-----------------|----------------|---------------|
| Pleural effusion                                |                 |                |               |
| subjects affected / exposed                     | 1 / 103 (0.97%) | 0 / 44 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0         |
| Pneumonitis                                     |                 |                |               |
| subjects affected / exposed                     | 0 / 103 (0.00%) | 0 / 44 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0         |
| Pulmonary embolism                              |                 |                |               |
| subjects affected / exposed                     | 0 / 103 (0.00%) | 0 / 44 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0         |
| Pulmonary haemorrhage                           |                 |                |               |
| subjects affected / exposed                     | 1 / 103 (0.97%) | 0 / 44 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0         |
| Respiratory distress                            |                 |                |               |
| subjects affected / exposed                     | 0 / 103 (0.00%) | 0 / 44 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0         |
| Psychiatric disorders                           |                 |                |               |
| Delirium  |                 |                |               |
| subjects affected / exposed                     | 0 / 103 (0.00%) | 1 / 44 (2.27%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0         |
| Mental status changes                           |                 |                |               |
| subjects affected / exposed                     | 1 / 103 (0.97%) | 0 / 44 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0         |
| Investigations                                  |                 |                |               |
| Blood urine present                             |                 |                |               |
| subjects affected / exposed                     | 0 / 103 (0.00%) | 1 / 44 (2.27%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0         |

|   |                 |                |               |
|---|-----------------|----------------|---------------|
| Blood creatinine increased<br>subjects affected / exposed       | 1 / 103 (0.97%) | 1 / 44 (2.27%) | 0 / 9 (0.00%) |
| occurrences causally related to<br>treatment / all              | 0 / 1           | 0 / 1          | 0 / 0         |
| deaths causally related to<br>treatment / all                   | 0 / 0           | 0 / 0          | 0 / 0         |
| Hepatic enzyme increased<br>subjects affected / exposed         | 1 / 103 (0.97%) | 0 / 44 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to<br>treatment / all              | 0 / 1           | 0 / 0          | 0 / 0         |
| deaths causally related to<br>treatment / all                   | 0 / 1           | 0 / 0          | 0 / 0         |
| Urine output decreased<br>subjects affected / exposed           | 1 / 103 (0.97%) | 0 / 44 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to<br>treatment / all              | 0 / 1           | 0 / 0          | 0 / 0         |
| deaths causally related to<br>treatment / all                   | 0 / 0           | 0 / 0          | 0 / 0         |
| White blood cell count increased<br>subjects affected / exposed | 0 / 103 (0.00%) | 1 / 44 (2.27%) | 0 / 9 (0.00%) |
| occurrences causally related to<br>treatment / all              | 0 / 0           | 0 / 1          | 0 / 0         |
| deaths causally related to<br>treatment / all                   | 0 / 0           | 0 / 0          | 0 / 0         |
| Injury, poisoning and procedural<br>complications               |                 |                |               |
| Anastomotic haemorrhage<br>subjects affected / exposed          | 1 / 103 (0.97%) | 0 / 44 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to<br>treatment / all              | 0 / 1           | 0 / 0          | 0 / 0         |
| deaths causally related to<br>treatment / all                   | 0 / 0           | 0 / 0          | 0 / 0         |
| Craniocerebral injury<br>subjects affected / exposed            | 0 / 103 (0.00%) | 0 / 44 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to<br>treatment / all              | 0 / 0           | 0 / 0          | 0 / 0         |
| deaths causally related to<br>treatment / all                   | 0 / 0           | 0 / 0          | 0 / 0         |
| Fall<br>subjects affected / exposed                             | 1 / 103 (0.97%) | 0 / 44 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to<br>treatment / all              | 0 / 1           | 0 / 0          | 0 / 0         |
| deaths causally related to<br>treatment / all                   | 0 / 0           | 0 / 0          | 0 / 0         |
| Fractured sacrum<br>subjects affected / exposed                 | 1 / 103 (0.97%) | 0 / 44 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to<br>treatment / all              | 0 / 1           | 0 / 0          | 0 / 0         |
| deaths causally related to<br>treatment / all                   | 0 / 0           | 0 / 0          | 0 / 0         |



|   |                 |                |               |
|---|-----------------|----------------|---------------|
| Spinal fracture                                 |                 |                |               |
| subjects affected / exposed                     | 1 / 103 (0.97%) | 0 / 44 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0         |
| Stomal hernia                                   |                 |                |               |
| subjects affected / exposed                     | 0 / 103 (0.00%) | 0 / 44 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0         |
| Subdural haematoma                              |                 |                |               |
| subjects affected / exposed                     | 1 / 103 (0.97%) | 0 / 44 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0         |
| Urinary tract stoma complication                |                 |                |               |
| subjects affected / exposed                     | 0 / 103 (0.00%) | 0 / 44 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0         |
| Urostomy complication                           |                 |                |               |
| subjects affected / exposed                     | 1 / 103 (0.97%) | 1 / 44 (2.27%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0         |
| Cardiac disorders                               |                 |                |               |
| Angina pectoris                                 |                 |                |               |
| subjects affected / exposed                     | 1 / 103 (0.97%) | 0 / 44 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0         |
| Cardiac failure                                 |                 |                |               |
| subjects affected / exposed                     | 0 / 103 (0.00%) | 0 / 44 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0         |
| Coronary artery stenosis                        |                 |                |               |
| subjects affected / exposed                     | 1 / 103 (0.97%) | 0 / 44 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0         |
| Pericardial effusion                            |                 |                |               |

|   |                 |                |               |
|---|-----------------|----------------|---------------|
| subjects affected / exposed                     | 0 / 103 (0.00%) | 1 / 44 (2.27%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 1 / 1          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0         |
| Nervous system disorders                        |                 |                |               |
| Cerebellar haemorrhage                          |                 |                |               |
| subjects affected / exposed                     | 0 / 103 (0.00%) | 0 / 44 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0         |
| Cerebrovascular accident                        |                 |                |               |
| subjects affected / exposed                     | 1 / 103 (0.97%) | 0 / 44 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 1 / 1           | 0 / 0          | 0 / 0         |
| Cognitive disorder                              |                 |                |               |
| subjects affected / exposed                     | 1 / 103 (0.97%) | 0 / 44 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 1           | 0 / 0          | 0 / 0         |
| Lethargy  |                 |                |               |
| subjects affected / exposed                     | 0 / 103 (0.00%) | 1 / 44 (2.27%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0         |
| Motor dysfunction                               |                 |                |               |
| subjects affected / exposed                     | 1 / 103 (0.97%) | 0 / 44 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0         |
| Peripheral nerve paresis                        |                 |                |               |
| subjects affected / exposed                     | 0 / 103 (0.00%) | 0 / 44 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0         |
| Sciatica  |                 |                |               |
| subjects affected / exposed                     | 0 / 103 (0.00%) | 1 / 44 (2.27%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0         |
| Spinal cord compression                         |                 |                |               |

|   |                 |                |               |
|---|-----------------|----------------|---------------|
| subjects affected / exposed                     | 2 / 103 (1.94%) | 0 / 44 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 1           | 0 / 0          | 0 / 0         |
| Syncope   |                 |                |               |
| subjects affected / exposed                     | 1 / 103 (0.97%) | 0 / 44 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0         |
| Blood and lymphatic system disorders            |                 |                |               |
| Anaemia   |                 |                |               |
| subjects affected / exposed                     | 0 / 103 (0.00%) | 1 / 44 (2.27%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0         |
| Leukocytosis                                    |                 |                |               |
| subjects affected / exposed                     | 0 / 103 (0.00%) | 0 / 44 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0         |
| Eye disorders                                   |                 |                |               |
| Chorioretinopathy                               |                 |                |               |
| subjects affected / exposed                     | 1 / 103 (0.97%) | 0 / 44 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0         |
| Detachment of retinal pigment epithelium        |                 |                |               |
| subjects affected / exposed                     | 0 / 103 (0.00%) | 0 / 44 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0         |
| Keratitis                                       |                 |                |               |
| subjects affected / exposed                     | 0 / 103 (0.00%) | 0 / 44 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0         |
| Optic neuropathy                                |                 |                |               |
| subjects affected / exposed                     | 1 / 103 (0.97%) | 0 / 44 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0         |

|   |                 |                |               |
|---|-----------------|----------------|---------------|
| Gastrointestinal disorders                      |                 |                |               |
| Abdominal distension                            |                 |                |               |
| subjects affected / exposed                     | 0 / 103 (0.00%) | 0 / 44 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0         |
| Abdominal pain                                  |                 |                |               |
| subjects affected / exposed                     | 2 / 103 (1.94%) | 1 / 44 (2.27%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 3           | 0 / 1          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0         |
| Constipation                                    |                 |                |               |
| subjects affected / exposed                     | 2 / 103 (1.94%) | 3 / 44 (6.82%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 3          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0         |
| Colitis   |                 |                |               |
| subjects affected / exposed                     | 1 / 103 (0.97%) | 0 / 44 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0         |
| Diarrhoea                                       |                 |                |               |
| subjects affected / exposed                     | 2 / 103 (1.94%) | 0 / 44 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 2 / 2           | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0         |
| Gastrointestinal obstruction                    |                 |                |               |
| subjects affected / exposed                     | 0 / 103 (0.00%) | 0 / 44 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0         |
| Haematemesis                                    |                 |                |               |
| subjects affected / exposed                     | 0 / 103 (0.00%) | 0 / 44 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0         |
| Intestinal infarction                           |                 |                |               |
| subjects affected / exposed                     | 1 / 103 (0.97%) | 0 / 44 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 1           | 0 / 0          | 0 / 0         |
| Intestinal obstruction                          |                 |                |               |

|   |                 |                |               |
|---|-----------------|----------------|---------------|
| subjects affected / exposed                     | 1 / 103 (0.97%) | 1 / 44 (2.27%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 4           | 0 / 1          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 1          | 0 / 0         |
| Large intestinal obstruction                    |                 |                |               |
| subjects affected / exposed                     | 0 / 103 (0.00%) | 1 / 44 (2.27%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0         |
| Nausea  |                 |                |               |
| subjects affected / exposed                     | 1 / 103 (0.97%) | 3 / 44 (6.82%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1           | 1 / 3          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0         |
| Oesophagitis                                    |                 |                |               |
| subjects affected / exposed                     | 0 / 103 (0.00%) | 0 / 44 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0         |
| Pancreatic mass                                 |                 |                |               |
| subjects affected / exposed                     | 0 / 103 (0.00%) | 0 / 44 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0         |
| Small intestinal obstruction                    |                 |                |               |
| subjects affected / exposed                     | 2 / 103 (1.94%) | 2 / 44 (4.55%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 2          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0         |
| Stomatitis                                      |                 |                |               |
| subjects affected / exposed                     | 0 / 103 (0.00%) | 0 / 44 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0         |
| Subileus  |                 |                |               |
| subjects affected / exposed                     | 0 / 103 (0.00%) | 0 / 44 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0         |
| Vomiting  |                 |                |               |

|   |                 |                |               |
|---|-----------------|----------------|---------------|
| subjects affected / exposed                     | 1 / 103 (0.97%) | 2 / 44 (4.55%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 2          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0         |
| <b>Hepatobiliary disorders</b>                  |                 |                |               |
| Cholecystitis acute                             |                 |                |               |
| subjects affected / exposed                     | 1 / 103 (0.97%) | 0 / 44 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0         |
| Gallbladder enlargement                         |                 |                |               |
| subjects affected / exposed                     | 0 / 103 (0.00%) | 1 / 44 (2.27%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 1 / 1          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0         |
| <b>Skin and subcutaneous tissue disorders</b>   |                 |                |               |
| Angioedema                                      |                 |                |               |
| subjects affected / exposed                     | 1 / 103 (0.97%) | 0 / 44 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0         |
| Skin toxicity                                   |                 |                |               |
| subjects affected / exposed                     | 0 / 103 (0.00%) | 0 / 44 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0         |
| <b>Renal and urinary disorders</b>              |                 |                |               |
| Acute kidney injury                             |                 |                |               |
| subjects affected / exposed                     | 3 / 103 (2.91%) | 4 / 44 (9.09%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 3           | 0 / 4          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 1          | 0 / 0         |
| Bladder outlet obstruction                      |                 |                |               |
| subjects affected / exposed                     | 1 / 103 (0.97%) | 0 / 44 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0         |
| Bladder mass                                    |                 |                |               |
| subjects affected / exposed                     | 0 / 103 (0.00%) | 0 / 44 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0         |

|   |                 |                |                |
|---|-----------------|----------------|----------------|
| Chronic kidney disease                          |                 |                |                |
| subjects affected / exposed                     | 0 / 103 (0.00%) | 1 / 44 (2.27%) | 0 / 9 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0          |
| Haematuria                                      |                 |                |                |
| subjects affected / exposed                     | 4 / 103 (3.88%) | 1 / 44 (2.27%) | 1 / 9 (11.11%) |
| occurrences causally related to treatment / all | 0 / 4           | 0 / 1          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0          |
| Hydronephrosis                                  |                 |                |                |
| subjects affected / exposed                     | 0 / 103 (0.00%) | 0 / 44 (0.00%) | 0 / 9 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0          |
| Renal failure                                   |                 |                |                |
| subjects affected / exposed                     | 0 / 103 (0.00%) | 0 / 44 (0.00%) | 0 / 9 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0          |
| Renal injury                                    |                 |                |                |
| subjects affected / exposed                     | 0 / 103 (0.00%) | 1 / 44 (2.27%) | 0 / 9 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0          |
| Urinary retention                               |                 |                |                |
| subjects affected / exposed                     | 1 / 103 (0.97%) | 1 / 44 (2.27%) | 0 / 9 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0          |
| Urinary tract obstruction                       |                 |                |                |
| subjects affected / exposed                     | 0 / 103 (0.00%) | 1 / 44 (2.27%) | 0 / 9 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0          |
| Endocrine disorders                             |                 |                |                |
| Hypercalcaemia of malignancy                    |                 |                |                |
| subjects affected / exposed                     | 0 / 103 (0.00%) | 0 / 44 (0.00%) | 0 / 9 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0          |
| Musculoskeletal and connective tissue           |                 |                |                |

|   |                 |                |               |
|---|-----------------|----------------|---------------|
| disorders                                       |                 |                |               |
| Arthralgia                                      |                 |                |               |
| subjects affected / exposed                     | 1 / 103 (0.97%) | 0 / 44 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0         |
| Back pain                                       |                 |                |               |
| subjects affected / exposed                     | 2 / 103 (1.94%) | 2 / 44 (4.55%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 2          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0         |
| Bone pain                                       |                 |                |               |
| subjects affected / exposed                     | 0 / 103 (0.00%) | 0 / 44 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0         |
| Flank pain                                      |                 |                |               |
| subjects affected / exposed                     | 1 / 103 (0.97%) | 0 / 44 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0         |
| Intervertebral disc protrusion                  |                 |                |               |
| subjects affected / exposed                     | 1 / 103 (0.97%) | 0 / 44 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0         |
| Muscular weakness                               |                 |                |               |
| subjects affected / exposed                     | 1 / 103 (0.97%) | 1 / 44 (2.27%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0         |
| Musculoskeletal chest pain                      |                 |                |               |
| subjects affected / exposed                     | 1 / 103 (0.97%) | 0 / 44 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0         |
| Musculoskeletal pain                            |                 |                |               |
| subjects affected / exposed                     | 0 / 103 (0.00%) | 1 / 44 (2.27%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0         |
| Infections and infestations                     |                 |                |               |



|   |                 |                |               |
|---|-----------------|----------------|---------------|
| Bacteraemia                                     |                 |                |               |
| subjects affected / exposed                     | 1 / 103 (0.97%) | 0 / 44 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0         |
| Bronchitis                                      |                 |                |               |
| subjects affected / exposed                     | 0 / 103 (0.00%) | 0 / 44 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0         |
| COVID-19  |                 |                |               |
| subjects affected / exposed                     | 0 / 103 (0.00%) | 0 / 44 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0         |
| Cytomegalovirus infection                       |                 |                |               |
| subjects affected / exposed                     | 0 / 103 (0.00%) | 0 / 44 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0         |
| Device related infection                        |                 |                |               |
| subjects affected / exposed                     | 0 / 103 (0.00%) | 1 / 44 (2.27%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0         |
| Empyema   |                 |                |               |
| subjects affected / exposed                     | 0 / 103 (0.00%) | 1 / 44 (2.27%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0         |
| Febrile infection                               |                 |                |               |
| subjects affected / exposed                     | 1 / 103 (0.97%) | 0 / 44 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0         |
| Gastroenteritis salmonella                      |                 |                |               |
| subjects affected / exposed                     | 0 / 103 (0.00%) | 0 / 44 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0         |
| Herpes simplex                                  |                 |                |               |

|   |                 |                |               |
|---|-----------------|----------------|---------------|
| subjects affected / exposed                     | 0 / 103 (0.00%) | 0 / 44 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0         |
| Pelvic abscess                                  |                 |                |               |
| subjects affected / exposed                     | 1 / 103 (0.97%) | 0 / 44 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0         |
| Pneumonia                                       |                 |                |               |
| subjects affected / exposed                     | 2 / 103 (1.94%) | 2 / 44 (4.55%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 3           | 0 / 2          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 1           | 0 / 0          | 0 / 0         |
| Pneumonia viral                                 |                 |                |               |
| subjects affected / exposed                     | 0 / 103 (0.00%) | 0 / 44 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0         |
| Pyelonephritis                                  |                 |                |               |
| subjects affected / exposed                     | 1 / 103 (0.97%) | 0 / 44 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0         |
| Pyelonephritis acute                            |                 |                |               |
| subjects affected / exposed                     | 1 / 103 (0.97%) | 0 / 44 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0         |
| Sepsis  |                 |                |               |
| subjects affected / exposed                     | 1 / 103 (0.97%) | 1 / 44 (2.27%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 1          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 1          | 0 / 0         |
| Septic shock                                    |                 |                |               |
| subjects affected / exposed                     | 1 / 103 (0.97%) | 0 / 44 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 1           | 0 / 0          | 0 / 0         |
| Spinal cord infection                           |                 |                |               |

|   |                 |                |                |
|---|-----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 103 (0.00%) | 0 / 44 (0.00%) | 1 / 9 (11.11%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0          |
| Urinary tract infection                         |                 |                |                |
| subjects affected / exposed                     | 6 / 103 (5.83%) | 1 / 44 (2.27%) | 0 / 9 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 6           | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0          |
| Urosepsis                                       |                 |                |                |
| subjects affected / exposed                     | 2 / 103 (1.94%) | 1 / 44 (2.27%) | 0 / 9 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0          |
| Viral oesophagitis                              |                 |                |                |
| subjects affected / exposed                     | 0 / 103 (0.00%) | 0 / 44 (0.00%) | 0 / 9 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0          |
| Wound infection                                 |                 |                |                |
| subjects affected / exposed                     | 0 / 103 (0.00%) | 1 / 44 (2.27%) | 0 / 9 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0          |
| Metabolism and nutrition disorders              |                 |                |                |
| Decreased appetite                              |                 |                |                |
| subjects affected / exposed                     | 1 / 103 (0.97%) | 1 / 44 (2.27%) | 0 / 9 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0          |
| Dehydration                                     |                 |                |                |
| subjects affected / exposed                     | 0 / 103 (0.00%) | 1 / 44 (2.27%) | 0 / 9 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0          |
| Failure to thrive                               |                 |                |                |
| subjects affected / exposed                     | 0 / 103 (0.00%) | 0 / 44 (0.00%) | 0 / 9 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0          |
| Hypercalcaemia                                  |                 |                |                |

|   |                 |                |               |
|---|-----------------|----------------|---------------|
| subjects affected / exposed                     | 2 / 103 (1.94%) | 0 / 44 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0         |
| Hyperkalaemia                                   |                 |                |               |
| subjects affected / exposed                     | 1 / 103 (0.97%) | 0 / 44 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0         |
| Hyperphosphataemia                              |                 |                |               |
| subjects affected / exposed                     | 1 / 103 (0.97%) | 0 / 44 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0         |
| Hypocalcaemia                                   |                 |                |               |
| subjects affected / exposed                     | 1 / 103 (0.97%) | 0 / 44 (0.00%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0         |
| Hyponatraemia                                   |                 |                |               |
| subjects affected / exposed                     | 0 / 103 (0.00%) | 2 / 44 (4.55%) | 0 / 9 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 1 / 2          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0         |

| Serious adverse events  | Cohort A-CD: FGFR3 mutations or fusions | Other-CD       |  |
|---|---|----------------|--|
| Total subjects affected by serious adverse events                   |   |                |  |
| subjects affected / exposed   | 48 / 101 (47.52%)                       | 1 / 3 (33.33%) |  |
| number of deaths (all causes)                                       | 83                                      | 2              |  |
| number of deaths resulting from adverse events                      | 16                                      | 0              |  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |   |                |  |
| Cancer pain   |   |                |  |
| subjects affected / exposed   | 0 / 101 (0.00%)                         | 0 / 3 (0.00%)  |  |
| occurrences causally related to treatment / all                     | 0 / 0                                   | 0 / 0          |  |
| deaths causally related to treatment / all                          | 0 / 0                                   | 0 / 0          |  |
| Lung adenocarcinoma   |   |                |  |
| subjects affected / exposed   | 0 / 101 (0.00%)                         | 0 / 3 (0.00%)  |  |
| occurrences causally related to treatment / all                     | 0 / 0                                   | 0 / 0          |  |
| deaths causally related to treatment / all                          | 0 / 0                                   | 0 / 0          |  |

|   |                 |               |  |
|---|-----------------|---------------|--|
| Malignant neoplasm progression<br>subjects affected / exposed | 0 / 101 (0.00%) | 0 / 3 (0.00%) |  |
| occurrences causally related to<br>treatment / all            | 0 / 0           | 0 / 0         |  |
| deaths causally related to<br>treatment / all                 | 0 / 0           | 0 / 0         |  |
| Rectal cancer<br>subjects affected / exposed                  | 1 / 101 (0.99%) | 0 / 3 (0.00%) |  |
| occurrences causally related to<br>treatment / all            | 0 / 1           | 0 / 0         |  |
| deaths causally related to<br>treatment / all                 | 0 / 0           | 0 / 0         |  |
| Tumour associated fever<br>subjects affected / exposed        | 1 / 101 (0.99%) | 0 / 3 (0.00%) |  |
| occurrences causally related to<br>treatment / all            | 0 / 1           | 0 / 0         |  |
| deaths causally related to<br>treatment / all                 | 0 / 0           | 0 / 0         |  |
| Tumour pain<br>subjects affected / exposed                    | 1 / 101 (0.99%) | 0 / 3 (0.00%) |  |
| occurrences causally related to<br>treatment / all            | 0 / 1           | 0 / 0         |  |
| deaths causally related to<br>treatment / all                 | 0 / 0           | 0 / 0         |  |
| Vascular disorders  |                 |               |  |
| Hypertension<br>subjects affected / exposed                   | 0 / 101 (0.00%) | 0 / 3 (0.00%) |  |
| occurrences causally related to<br>treatment / all            | 0 / 0           | 0 / 0         |  |
| deaths causally related to<br>treatment / all                 | 0 / 0           | 0 / 0         |  |
| Hypotension<br>subjects affected / exposed                    | 0 / 101 (0.00%) | 0 / 3 (0.00%) |  |
| occurrences causally related to<br>treatment / all            | 0 / 0           | 0 / 0         |  |
| deaths causally related to<br>treatment / all                 | 0 / 0           | 0 / 0         |  |
| Hypovolaemic shock<br>subjects affected / exposed             | 1 / 101 (0.99%) | 0 / 3 (0.00%) |  |
| occurrences causally related to<br>treatment / all            | 0 / 1           | 0 / 0         |  |
| deaths causally related to<br>treatment / all                 | 0 / 1           | 0 / 0         |  |
| Phlebitis<br>subjects affected / exposed                      | 0 / 101 (0.00%) | 0 / 3 (0.00%) |  |
| occurrences causally related to<br>treatment / all            | 0 / 0           | 0 / 0         |  |
| deaths causally related to<br>treatment / all                 | 0 / 0           | 0 / 0         |  |
| Vasculitis necrotising  |                 |               |  |

|  |                 |               |  |
|--|-----------------|---------------|--|
| subjects affected / exposed                          | 0 / 101 (0.00%) | 0 / 3 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0         |  |
| Venous thrombosis                                    |                 |               |  |
| subjects affected / exposed                          | 0 / 101 (0.00%) | 0 / 3 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0         |  |
| General disorders and administration site conditions |                 |               |  |
| Asthenia   |                 |               |  |
| subjects affected / exposed                          | 1 / 101 (0.99%) | 0 / 3 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 1           | 0 / 0         |  |
| deaths causally related to treatment / all           | 0 / 1           | 0 / 0         |  |
| Catheter site inflammation                           |                 |               |  |
| subjects affected / exposed                          | 1 / 101 (0.99%) | 0 / 3 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 1           | 0 / 0         |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0         |  |
| Disease progression                                  |                 |               |  |
| subjects affected / exposed                          | 2 / 101 (1.98%) | 0 / 3 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 2           | 0 / 0         |  |
| deaths causally related to treatment / all           | 0 / 2           | 0 / 0         |  |
| Fatigue  |                 |               |  |
| subjects affected / exposed                          | 0 / 101 (0.00%) | 0 / 3 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0         |  |
| Gait disturbance                                     |                 |               |  |
| subjects affected / exposed                          | 0 / 101 (0.00%) | 0 / 3 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0         |  |
| General physical health deterioration                |                 |               |  |
| subjects affected / exposed                          | 5 / 101 (4.95%) | 0 / 3 (0.00%) |  |
| occurrences causally related to treatment / all      | 1 / 5           | 0 / 0         |  |
| deaths causally related to treatment / all           | 0 / 3           | 0 / 0         |  |
| Malaise  |                 |               |  |

|   |                 |               |  |
|---|-----------------|---------------|--|
| subjects affected / exposed                     | 0 / 101 (0.00%) | 0 / 3 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Pain  |                 |               |  |
| subjects affected / exposed                     | 0 / 101 (0.00%) | 0 / 3 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Polyp   |                 |               |  |
| subjects affected / exposed                     | 0 / 101 (0.00%) | 0 / 3 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Pyrexia   |                 |               |  |
| subjects affected / exposed                     | 1 / 101 (0.99%) | 0 / 3 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Sudden death                                    |                 |               |  |
| subjects affected / exposed                     | 1 / 101 (0.99%) | 0 / 3 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0         |  |
| deaths causally related to treatment / all      | 1 / 1           | 0 / 0         |  |
| Systemic inflammatory response syndrome         |                 |               |  |
| subjects affected / exposed                     | 0 / 101 (0.00%) | 0 / 3 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Immune system disorders                         |                 |               |  |
| Anaphylactic shock                              |                 |               |  |
| subjects affected / exposed                     | 1 / 101 (0.99%) | 0 / 3 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Respiratory, thoracic and mediastinal disorders |                 |               |  |
| Cough   |                 |               |  |
| subjects affected / exposed                     | 0 / 101 (0.00%) | 0 / 3 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |

|   |                 |               |  |
|---|-----------------|---------------|--|
| Dyspnoea  |                 |               |  |
| subjects affected / exposed                     | 0 / 101 (0.00%) | 0 / 3 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Dyspnoea exertional                             |                 |               |  |
| subjects affected / exposed                     | 0 / 101 (0.00%) | 0 / 3 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Hiccups   |                 |               |  |
| subjects affected / exposed                     | 0 / 101 (0.00%) | 0 / 3 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Hypoxia   |                 |               |  |
| subjects affected / exposed                     | 0 / 101 (0.00%) | 0 / 3 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Pleural effusion                                |                 |               |  |
| subjects affected / exposed                     | 1 / 101 (0.99%) | 0 / 3 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Pneumonitis                                     |                 |               |  |
| subjects affected / exposed                     | 1 / 101 (0.99%) | 0 / 3 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Pulmonary embolism                              |                 |               |  |
| subjects affected / exposed                     | 1 / 101 (0.99%) | 0 / 3 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Pulmonary haemorrhage                           |                 |               |  |
| subjects affected / exposed                     | 0 / 101 (0.00%) | 0 / 3 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Respiratory distress                            |                 |               |  |



|   |                 |               |  |
|---|-----------------|---------------|--|
| subjects affected / exposed                     | 1 / 101 (0.99%) | 0 / 3 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 1           | 0 / 0         |  |
| Psychiatric disorders                           |                 |               |  |
| Delirium  |                 |               |  |
| subjects affected / exposed                     | 0 / 101 (0.00%) | 0 / 3 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Mental status changes                           |                 |               |  |
| subjects affected / exposed                     | 0 / 101 (0.00%) | 0 / 3 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Investigations                                  |                 |               |  |
| Blood urine present                             |                 |               |  |
| subjects affected / exposed                     | 0 / 101 (0.00%) | 0 / 3 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Blood creatinine increased                      |                 |               |  |
| subjects affected / exposed                     | 1 / 101 (0.99%) | 0 / 3 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0         |  |
| deaths causally related to treatment / all      | 1 / 1           | 0 / 0         |  |
| Hepatic enzyme increased                        |                 |               |  |
| subjects affected / exposed                     | 0 / 101 (0.00%) | 0 / 3 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Urine output decreased                          |                 |               |  |
| subjects affected / exposed                     | 0 / 101 (0.00%) | 0 / 3 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| White blood cell count increased                |                 |               |  |
| subjects affected / exposed                     | 0 / 101 (0.00%) | 0 / 3 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Injury, poisoning and procedural                |                 |               |  |

|   |                 |               |  |  |
|---|-----------------|---------------|--|--|
| complications                                   |                 |               |  |  |
| Anastomotic haemorrhage                         |                 |               |  |  |
| subjects affected / exposed                     | 0 / 101 (0.00%) | 0 / 3 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |  |
| Craniocerebral injury                           |                 |               |  |  |
| subjects affected / exposed                     | 1 / 101 (0.99%) | 0 / 3 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |  |
| Fall  |                 |               |  |  |
| subjects affected / exposed                     | 0 / 101 (0.00%) | 0 / 3 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |  |
| Fractured sacrum                                |                 |               |  |  |
| subjects affected / exposed                     | 0 / 101 (0.00%) | 0 / 3 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |  |
| Spinal fracture                                 |                 |               |  |  |
| subjects affected / exposed                     | 0 / 101 (0.00%) | 0 / 3 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |  |
| Stomal hernia                                   |                 |               |  |  |
| subjects affected / exposed                     | 1 / 101 (0.99%) | 0 / 3 (0.00%) |  |  |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |  |
| Subdural haematoma                              |                 |               |  |  |
| subjects affected / exposed                     | 0 / 101 (0.00%) | 0 / 3 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |  |
| Urinary tract stoma complication                |                 |               |  |  |
| subjects affected / exposed                     | 1 / 101 (0.99%) | 0 / 3 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |  |
| Urostomy complication                           |                 |               |  |  |

|   |                 |               |  |
|---|-----------------|---------------|--|
| subjects affected / exposed                     | 0 / 101 (0.00%) | 0 / 3 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Cardiac disorders                               |                 |               |  |
| Angina pectoris                                 |                 |               |  |
| subjects affected / exposed                     | 0 / 101 (0.00%) | 0 / 3 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Cardiac failure                                 |                 |               |  |
| subjects affected / exposed                     | 1 / 101 (0.99%) | 0 / 3 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 1           | 0 / 0         |  |
| Coronary artery stenosis                        |                 |               |  |
| subjects affected / exposed                     | 0 / 101 (0.00%) | 0 / 3 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Pericardial effusion                            |                 |               |  |
| subjects affected / exposed                     | 0 / 101 (0.00%) | 0 / 3 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Nervous system disorders                        |                 |               |  |
| Cerebellar haemorrhage                          |                 |               |  |
| subjects affected / exposed                     | 1 / 101 (0.99%) | 0 / 3 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Cerebrovascular accident                        |                 |               |  |
| subjects affected / exposed                     | 0 / 101 (0.00%) | 0 / 3 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Cognitive disorder                              |                 |               |  |
| subjects affected / exposed                     | 1 / 101 (0.99%) | 0 / 3 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Lethargy  |                 |               |  |

|   |                 |                |  |
|---|-----------------|----------------|--|
| subjects affected / exposed                     | 0 / 101 (0.00%) | 0 / 3 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Motor dysfunction                               |                 |                |  |
| subjects affected / exposed                     | 0 / 101 (0.00%) | 0 / 3 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Peripheral nerve paresis                        |                 |                |  |
| subjects affected / exposed                     | 1 / 101 (0.99%) | 0 / 3 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Sciatica  |                 |                |  |
| subjects affected / exposed                     | 0 / 101 (0.00%) | 0 / 3 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Spinal cord compression                         |                 |                |  |
| subjects affected / exposed                     | 0 / 101 (0.00%) | 0 / 3 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Syncope   |                 |                |  |
| subjects affected / exposed                     | 0 / 101 (0.00%) | 0 / 3 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Blood and lymphatic system disorders            |                 |                |  |
| Anaemia   |                 |                |  |
| subjects affected / exposed                     | 2 / 101 (1.98%) | 1 / 3 (33.33%) |  |
| occurrences causally related to treatment / all | 2 / 2           | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Leukocytosis                                    |                 |                |  |
| subjects affected / exposed                     | 1 / 101 (0.99%) | 0 / 3 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Eye disorders                                   |                 |                |  |

|   |                 |               |  |
|---|-----------------|---------------|--|
| Chorioretinopathy                               |                 |               |  |
| subjects affected / exposed                     | 0 / 101 (0.00%) | 0 / 3 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Detachment of retinal pigment epithelium        |                 |               |  |
| subjects affected / exposed                     | 1 / 101 (0.99%) | 0 / 3 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Keratitis                                       |                 |               |  |
| subjects affected / exposed                     | 1 / 101 (0.99%) | 0 / 3 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Optic neuropathy                                |                 |               |  |
| subjects affected / exposed                     | 0 / 101 (0.00%) | 0 / 3 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Gastrointestinal disorders                      |                 |               |  |
| Abdominal distension                            |                 |               |  |
| subjects affected / exposed                     | 1 / 101 (0.99%) | 0 / 3 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Abdominal pain                                  |                 |               |  |
| subjects affected / exposed                     | 1 / 101 (0.99%) | 0 / 3 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Constipation                                    |                 |               |  |
| subjects affected / exposed                     | 0 / 101 (0.00%) | 0 / 3 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Colitis   |                 |               |  |
| subjects affected / exposed                     | 0 / 101 (0.00%) | 0 / 3 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |

|   |                 |               |  |
|---|-----------------|---------------|--|
| Diarrhoea                                       |                 |               |  |
| subjects affected / exposed                     | 0 / 101 (0.00%) | 0 / 3 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Gastrointestinal obstruction                    |                 |               |  |
| subjects affected / exposed                     | 1 / 101 (0.99%) | 0 / 3 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Haematemesis                                    |                 |               |  |
| subjects affected / exposed                     | 1 / 101 (0.99%) | 0 / 3 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Intestinal infarction                           |                 |               |  |
| subjects affected / exposed                     | 0 / 101 (0.00%) | 0 / 3 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Intestinal obstruction                          |                 |               |  |
| subjects affected / exposed                     | 1 / 101 (0.99%) | 0 / 3 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Large intestinal obstruction                    |                 |               |  |
| subjects affected / exposed                     | 0 / 101 (0.00%) | 0 / 3 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Nausea  |                 |               |  |
| subjects affected / exposed                     | 0 / 101 (0.00%) | 0 / 3 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Oesophagitis                                    |                 |               |  |
| subjects affected / exposed                     | 1 / 101 (0.99%) | 0 / 3 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Pancreatic mass                                 |                 |               |  |

|   |                 |               |  |
|---|-----------------|---------------|--|
| subjects affected / exposed                     | 1 / 101 (0.99%) | 0 / 3 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Small intestinal obstruction                    |                 |               |  |
| subjects affected / exposed                     | 0 / 101 (0.00%) | 0 / 3 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Stomatitis                                      |                 |               |  |
| subjects affected / exposed                     | 1 / 101 (0.99%) | 0 / 3 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Subileus  |                 |               |  |
| subjects affected / exposed                     | 2 / 101 (1.98%) | 0 / 3 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Vomiting  |                 |               |  |
| subjects affected / exposed                     | 0 / 101 (0.00%) | 0 / 3 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Hepatobiliary disorders                         |                 |               |  |
| Cholecystitis acute                             |                 |               |  |
| subjects affected / exposed                     | 0 / 101 (0.00%) | 0 / 3 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Gallbladder enlargement                         |                 |               |  |
| subjects affected / exposed                     | 0 / 101 (0.00%) | 0 / 3 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Skin and subcutaneous tissue disorders          |                 |               |  |
| Angioedema                                      |                 |               |  |
| subjects affected / exposed                     | 0 / 101 (0.00%) | 0 / 3 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Skin toxicity                                   |                 |               |  |

|   |                 |               |  |
|---|-----------------|---------------|--|
| subjects affected / exposed                     | 1 / 101 (0.99%) | 0 / 3 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Renal and urinary disorders                     |                 |               |  |
| Acute kidney injury                             |                 |               |  |
| subjects affected / exposed                     | 2 / 101 (1.98%) | 0 / 3 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Bladder outlet obstruction                      |                 |               |  |
| subjects affected / exposed                     | 0 / 101 (0.00%) | 0 / 3 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Bladder mass                                    |                 |               |  |
| subjects affected / exposed                     | 1 / 101 (0.99%) | 0 / 3 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Chronic kidney disease                          |                 |               |  |
| subjects affected / exposed                     | 0 / 101 (0.00%) | 0 / 3 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Haematuria                                      |                 |               |  |
| subjects affected / exposed                     | 0 / 101 (0.00%) | 0 / 3 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Hydronephrosis                                  |                 |               |  |
| subjects affected / exposed                     | 2 / 101 (1.98%) | 0 / 3 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 1           | 0 / 0         |  |
| Renal failure                                   |                 |               |  |
| subjects affected / exposed                     | 3 / 101 (2.97%) | 0 / 3 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 3           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 1           | 0 / 0         |  |
| Renal injury                                    |                 |               |  |



|   |                 |                |  |
|---|-----------------|----------------|--|
| subjects affected / exposed                     | 0 / 101 (0.00%) | 0 / 3 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Urinary retention                               |                 |                |  |
| subjects affected / exposed                     | 0 / 101 (0.00%) | 0 / 3 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Urinary tract obstruction                       |                 |                |  |
| subjects affected / exposed                     | 0 / 101 (0.00%) | 0 / 3 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Endocrine disorders                             |                 |                |  |
| Hypercalcaemia of malignancy                    |                 |                |  |
| subjects affected / exposed                     | 1 / 101 (0.99%) | 0 / 3 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Musculoskeletal and connective tissue disorders |                 |                |  |
| Arthralgia                                      |                 |                |  |
| subjects affected / exposed                     | 0 / 101 (0.00%) | 0 / 3 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Back pain                                       |                 |                |  |
| subjects affected / exposed                     | 1 / 101 (0.99%) | 1 / 3 (33.33%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Bone pain                                       |                 |                |  |
| subjects affected / exposed                     | 1 / 101 (0.99%) | 0 / 3 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |
| Flank pain                                      |                 |                |  |
| subjects affected / exposed                     | 1 / 101 (0.99%) | 0 / 3 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |

|   |                 |               |  |
|---|-----------------|---------------|--|
| Intervertebral disc protrusion                  |                 |               |  |
| subjects affected / exposed                     | 0 / 101 (0.00%) | 0 / 3 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Muscular weakness                               |                 |               |  |
| subjects affected / exposed                     | 0 / 101 (0.00%) | 0 / 3 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Musculoskeletal chest pain                      |                 |               |  |
| subjects affected / exposed                     | 0 / 101 (0.00%) | 0 / 3 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Musculoskeletal pain                            |                 |               |  |
| subjects affected / exposed                     | 0 / 101 (0.00%) | 0 / 3 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Infections and infestations                     |                 |               |  |
| Bacteraemia                                     |                 |               |  |
| subjects affected / exposed                     | 0 / 101 (0.00%) | 0 / 3 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Bronchitis                                      |                 |               |  |
| subjects affected / exposed                     | 1 / 101 (0.99%) | 0 / 3 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 1           | 0 / 0         |  |
| COVID-19  |                 |               |  |
| subjects affected / exposed                     | 1 / 101 (0.99%) | 0 / 3 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Cytomegalovirus infection                       |                 |               |  |
| subjects affected / exposed                     | 1 / 101 (0.99%) | 0 / 3 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Device related infection                        |                 |               |  |

|   |                 |               |  |
|---|-----------------|---------------|--|
| subjects affected / exposed                     | 2 / 101 (1.98%) | 0 / 3 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Empyema   |                 |               |  |
| subjects affected / exposed                     | 0 / 101 (0.00%) | 0 / 3 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Febrile infection                               |                 |               |  |
| subjects affected / exposed                     | 0 / 101 (0.00%) | 0 / 3 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Gastroenteritis salmonella                      |                 |               |  |
| subjects affected / exposed                     | 1 / 101 (0.99%) | 0 / 3 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Herpes simplex                                  |                 |               |  |
| subjects affected / exposed                     | 1 / 101 (0.99%) | 0 / 3 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Pelvic abscess                                  |                 |               |  |
| subjects affected / exposed                     | 0 / 101 (0.00%) | 0 / 3 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Pneumonia                                       |                 |               |  |
| subjects affected / exposed                     | 0 / 101 (0.00%) | 0 / 3 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Pneumonia viral                                 |                 |               |  |
| subjects affected / exposed                     | 1 / 101 (0.99%) | 0 / 3 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Pyelonephritis                                  |                 |               |  |

|   |                 |               |  |
|---|-----------------|---------------|--|
| subjects affected / exposed                     | 1 / 101 (0.99%) | 0 / 3 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Pyelonephritis acute                            |                 |               |  |
| subjects affected / exposed                     | 0 / 101 (0.00%) | 0 / 3 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Sepsis  |                 |               |  |
| subjects affected / exposed                     | 2 / 101 (1.98%) | 0 / 3 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 1           | 0 / 0         |  |
| Septic shock                                    |                 |               |  |
| subjects affected / exposed                     | 0 / 101 (0.00%) | 0 / 3 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Spinal cord infection                           |                 |               |  |
| subjects affected / exposed                     | 0 / 101 (0.00%) | 0 / 3 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Urinary tract infection                         |                 |               |  |
| subjects affected / exposed                     | 8 / 101 (7.92%) | 0 / 3 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 11          | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Urosepsis                                       |                 |               |  |
| subjects affected / exposed                     | 0 / 101 (0.00%) | 0 / 3 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Viral oesophagitis                              |                 |               |  |
| subjects affected / exposed                     | 1 / 101 (0.99%) | 0 / 3 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Wound infection                                 |                 |               |  |

|   |                 |               |  |
|---|-----------------|---------------|--|
| subjects affected / exposed                     | 0 / 101 (0.00%) | 0 / 3 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Metabolism and nutrition disorders              |                 |               |  |
| Decreased appetite                              |                 |               |  |
| subjects affected / exposed                     | 1 / 101 (0.99%) | 0 / 3 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Dehydration                                     |                 |               |  |
| subjects affected / exposed                     | 0 / 101 (0.00%) | 0 / 3 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Failure to thrive                               |                 |               |  |
| subjects affected / exposed                     | 1 / 101 (0.99%) | 0 / 3 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 1           | 0 / 0         |  |
| Hypercalcaemia                                  |                 |               |  |
| subjects affected / exposed                     | 1 / 101 (0.99%) | 0 / 3 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Hyperkalaemia                                   |                 |               |  |
| subjects affected / exposed                     | 0 / 101 (0.00%) | 0 / 3 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Hyperphosphataemia                              |                 |               |  |
| subjects affected / exposed                     | 0 / 101 (0.00%) | 0 / 3 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Hypocalcaemia                                   |                 |               |  |
| subjects affected / exposed                     | 1 / 101 (0.99%) | 0 / 3 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Hyponatraemia                                   |                 |               |  |

|   |                 |                |  |
|---|-----------------|----------------|--|
| subjects affected / exposed                     | 1 / 101 (0.99%) | 1 / 3 (33.33%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 2          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          |  |

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

| <b>Non-serious adverse events</b>                     | Cohort A-ID: FGFR3 mutations or fusions | Cohort B-ID: All other FGF/FGFR alterations | Other-ID        |
|---|---|---|-----------------|
| Total subjects affected by non-serious adverse events |   |   |                 |
| subjects affected / exposed                           | 101 / 103 (98.06%)                      | 43 / 44 (97.73%)                            | 9 / 9 (100.00%) |
| Vascular disorders                                    |   |   |                 |
| Hypotension   |   |   |                 |
| subjects affected / exposed                           | 10 / 103 (9.71%)                        | 3 / 44 (6.82%)                              | 0 / 9 (0.00%)   |
| occurrences (all)                                     | 11                                      | 3   | 0               |
| Orthostatic hypotension                               |   |   |                 |
| subjects affected / exposed                           | 1 / 103 (0.97%)                         | 0 / 44 (0.00%)                              | 1 / 9 (11.11%)  |
| occurrences (all)                                     | 1                                       | 0   | 1               |
| General disorders and administration site conditions  |   |   |                 |
| Asthenia  |   |   |                 |
| subjects affected / exposed                           | 28 / 103 (27.18%)                       | 9 / 44 (20.45%)                             | 2 / 9 (22.22%)  |
| occurrences (all)                                     | 31                                      | 9   | 2               |
| Chills  |   |   |                 |
| subjects affected / exposed                           | 2 / 103 (1.94%)                         | 3 / 44 (6.82%)                              | 0 / 9 (0.00%)   |
| occurrences (all)                                     | 2                                       | 3   | 0               |
| Chest pain  |   |   |                 |
| subjects affected / exposed                           | 2 / 103 (1.94%)                         | 1 / 44 (2.27%)                              | 1 / 9 (11.11%)  |
| occurrences (all)                                     | 2                                       | 1   | 1               |
| Fatigue   |   |   |                 |
| subjects affected / exposed                           | 36 / 103 (34.95%)                       | 16 / 44 (36.36%)                            | 3 / 9 (33.33%)  |
| occurrences (all)                                     | 44                                      | 17  | 3               |
| Influenza like illness                                |   |   |                 |
| subjects affected / exposed                           | 2 / 103 (1.94%)                         | 1 / 44 (2.27%)                              | 1 / 9 (11.11%)  |
| occurrences (all)                                     | 2                                       | 2   | 1               |
| Mucosal inflammation                                  |   |   |                 |

|  |                         |                      |                     |
|--|-------------------------|----------------------|---------------------|
| subjects affected / exposed<br>occurrences (all)   | 2 / 103 (1.94%)<br>2    | 0 / 44 (0.00%)<br>0  | 1 / 9 (11.11%)<br>2 |
| Oedema peripheral<br>subjects affected / exposed<br>occurrences (all)  | 6 / 103 (5.83%)<br>6    | 8 / 44 (18.18%)<br>9 | 0 / 9 (0.00%)<br>0  |
| Pain<br>subjects affected / exposed<br>occurrences (all)   | 6 / 103 (5.83%)<br>6    | 3 / 44 (6.82%)<br>3  | 2 / 9 (22.22%)<br>2 |
| Pyrexia<br>subjects affected / exposed<br>occurrences (all)  | 14 / 103 (13.59%)<br>19 | 6 / 44 (13.64%)<br>6 | 0 / 9 (0.00%)<br>0  |
| Reproductive system and breast disorders<br>Pelvic pain<br>subjects affected / exposed<br>occurrences (all)  | 3 / 103 (2.91%)<br>3    | 3 / 44 (6.82%)<br>3  | 0 / 9 (0.00%)<br>0  |
| Respiratory, thoracic and mediastinal disorders<br>Cough<br>subjects affected / exposed<br>occurrences (all) | 15 / 103 (14.56%)<br>18 | 3 / 44 (6.82%)<br>3  | 0 / 9 (0.00%)<br>0  |
| Dyspnoea<br>subjects affected / exposed<br>occurrences (all)   | 4 / 103 (3.88%)<br>4    | 3 / 44 (6.82%)<br>4  | 1 / 9 (11.11%)<br>1 |
| Dysphonia<br>subjects affected / exposed<br>occurrences (all)  | 5 / 103 (4.85%)<br>5    | 4 / 44 (9.09%)<br>6  | 1 / 9 (11.11%)<br>1 |
| Epistaxis<br>subjects affected / exposed<br>occurrences (all)  | 13 / 103 (12.62%)<br>15 | 3 / 44 (6.82%)<br>3  | 2 / 9 (22.22%)<br>2 |
| Nasal dryness<br>subjects affected / exposed<br>occurrences (all)  | 3 / 103 (2.91%)<br>3    | 0 / 44 (0.00%)<br>0  | 2 / 9 (22.22%)<br>2 |
| Oropharyngeal pain<br>subjects affected / exposed<br>occurrences (all)                                       | 6 / 103 (5.83%)<br>7    | 3 / 44 (6.82%)<br>3  | 0 / 9 (0.00%)<br>0  |
| Upper-airway cough syndrome  |                         |                      |                     |

|  |                      |                     |                    |
|--|----------------------|---------------------|--------------------|
| subjects affected / exposed<br>occurrences (all) | 1 / 103 (0.97%)<br>1 | 0 / 44 (0.00%)<br>0 | 0 / 9 (0.00%)<br>0 |
| Psychiatric disorders                            |                      |                     |                    |
| Anxiety  |                      |                     |                    |
| subjects affected / exposed                      | 5 / 103 (4.85%)      | 1 / 44 (2.27%)      | 1 / 9 (11.11%)     |
| occurrences (all)                                | 6                    | 1                   | 1                  |
| Insomnia   |                      |                     |                    |
| subjects affected / exposed                      | 12 / 103 (11.65%)    | 1 / 44 (2.27%)      | 0 / 9 (0.00%)      |
| occurrences (all)                                | 13                   | 1                   | 0                  |
| Investigations                                   |                      |                     |                    |
| Alanine aminotransferase increased               |                      |                     |                    |
| subjects affected / exposed                      | 3 / 103 (2.91%)      | 1 / 44 (2.27%)      | 0 / 9 (0.00%)      |
| occurrences (all)                                | 3                    | 1                   | 0                  |
| Aspartate aminotransferase increased             |                      |                     |                    |
| subjects affected / exposed                      | 5 / 103 (4.85%)      | 0 / 44 (0.00%)      | 0 / 9 (0.00%)      |
| occurrences (all)                                | 6                    | 0                   | 0                  |
| Blood creatinine increased                       |                      |                     |                    |
| subjects affected / exposed                      | 17 / 103 (16.50%)    | 5 / 44 (11.36%)     | 2 / 9 (22.22%)     |
| occurrences (all)                                | 19                   | 5                   | 2                  |
| Blood phosphorus increased                       |                      |                     |                    |
| subjects affected / exposed                      | 9 / 103 (8.74%)      | 4 / 44 (9.09%)      | 2 / 9 (22.22%)     |
| occurrences (all)                                | 11                   | 6                   | 2                  |
| Lymphocyte count decreased                       |                      |                     |                    |
| subjects affected / exposed                      | 3 / 103 (2.91%)      | 6 / 44 (13.64%)     | 0 / 9 (0.00%)      |
| occurrences (all)                                | 3                    | 7                   | 0                  |
| Vitamin D decreased                              |                      |                     |                    |
| subjects affected / exposed                      | 3 / 103 (2.91%)      | 1 / 44 (2.27%)      | 1 / 9 (11.11%)     |
| occurrences (all)                                | 3                    | 1                   | 1                  |
| Weight decreased                                 |                      |                     |                    |
| subjects affected / exposed                      | 19 / 103 (18.45%)    | 2 / 44 (4.55%)      | 1 / 9 (11.11%)     |
| occurrences (all)                                | 21                   | 2                   | 1                  |
| Injury, poisoning and procedural complications   |                      |                     |                    |
| Contusion  |                      |                     |                    |
| subjects affected / exposed                      | 1 / 103 (0.97%)      | 0 / 44 (0.00%)      | 0 / 9 (0.00%)      |
| occurrences (all)                                | 1                    | 0                   | 0                  |
| Skin abrasion                                    |                      |                     |                    |



|  |                         |                       |                     |
|--|-------------------------|-----------------------|---------------------|
| subjects affected / exposed<br>occurrences (all)                             | 1 / 103 (0.97%)<br>1    | 0 / 44 (0.00%)<br>0   | 1 / 9 (11.11%)<br>1 |
| Cardiac disorders  |                         |                       |                     |
| Bundle branch block left<br>subjects affected / exposed<br>occurrences (all) | 0 / 103 (0.00%)<br>0    | 0 / 44 (0.00%)<br>0   | 0 / 9 (0.00%)<br>0  |
| Nervous system disorders   |                         |                       |                     |
| Ageusia<br>subjects affected / exposed<br>occurrences (all)                  | 6 / 103 (5.83%)<br>6    | 0 / 44 (0.00%)<br>0   | 1 / 9 (11.11%)<br>1 |
| Cognitive disorder<br>subjects affected / exposed<br>occurrences (all)       | 1 / 103 (0.97%)<br>1    | 0 / 44 (0.00%)<br>0   | 1 / 9 (11.11%)<br>1 |
| Dizziness<br>subjects affected / exposed<br>occurrences (all)                | 12 / 103 (11.65%)<br>14 | 4 / 44 (9.09%)<br>4   | 1 / 9 (11.11%)<br>2 |
| Disturbance in attention<br>subjects affected / exposed<br>occurrences (all) | 0 / 103 (0.00%)<br>0    | 0 / 44 (0.00%)<br>0   | 1 / 9 (11.11%)<br>1 |
| Dysgeusia<br>subjects affected / exposed<br>occurrences (all)                | 32 / 103 (31.07%)<br>35 | 9 / 44 (20.45%)<br>10 | 6 / 9 (66.67%)<br>6 |
| Headache<br>subjects affected / exposed<br>occurrences (all)                 | 6 / 103 (5.83%)<br>6    | 5 / 44 (11.36%)<br>5  | 0 / 9 (0.00%)<br>0  |
| Hypoaesthesia<br>subjects affected / exposed<br>occurrences (all)            | 1 / 103 (0.97%)<br>1    | 1 / 44 (2.27%)<br>1   | 0 / 9 (0.00%)<br>0  |
| Lethargy<br>subjects affected / exposed<br>occurrences (all)                 | 0 / 103 (0.00%)<br>0    | 1 / 44 (2.27%)<br>1   | 1 / 9 (11.11%)<br>1 |
| Neuropathy peripheral<br>subjects affected / exposed<br>occurrences (all)    | 4 / 103 (3.88%)<br>4    | 2 / 44 (4.55%)<br>2   | 1 / 9 (11.11%)<br>1 |
| Peripheral sensory neuropathy  |                         |                       |                     |

|  |                   |                  |                |
|--|-------------------|------------------|----------------|
| subjects affected / exposed                      | 1 / 103 (0.97%)   | 0 / 44 (0.00%)   | 1 / 9 (11.11%) |
| occurrences (all)                                | 1                 | 0                | 1              |
| Transient ischaemic attack                       |                   |                  |                |
| subjects affected / exposed                      | 0 / 103 (0.00%)   | 0 / 44 (0.00%)   | 1 / 9 (11.11%) |
| occurrences (all)                                | 0                 | 0                | 1              |
| Blood and lymphatic system disorders             |                   |                  |                |
| Anaemia  |                   |                  |                |
| subjects affected / exposed                      | 19 / 103 (18.45%) | 10 / 44 (22.73%) | 1 / 9 (11.11%) |
| occurrences (all)                                | 22                | 10               | 1              |
| Iron deficiency anaemia                          |                   |                  |                |
| subjects affected / exposed                      | 0 / 103 (0.00%)   | 0 / 44 (0.00%)   | 0 / 9 (0.00%)  |
| occurrences (all)                                | 0                 | 0                | 0              |
| Eye disorders                                    |                   |                  |                |
| Arcus lipoides                                   |                   |                  |                |
| subjects affected / exposed                      | 1 / 103 (0.97%)   | 0 / 44 (0.00%)   | 0 / 9 (0.00%)  |
| occurrences (all)                                | 1                 | 0                | 0              |
| Blepharitis                                      |                   |                  |                |
| subjects affected / exposed                      | 8 / 103 (7.77%)   | 1 / 44 (2.27%)   | 0 / 9 (0.00%)  |
| occurrences (all)                                | 10                | 1                | 0              |
| Cataract   |                   |                  |                |
| subjects affected / exposed                      | 6 / 103 (5.83%)   | 1 / 44 (2.27%)   | 0 / 9 (0.00%)  |
| occurrences (all)                                | 7                 | 1                | 0              |
| Corneal neovascularisation                       |                   |                  |                |
| subjects affected / exposed                      | 1 / 103 (0.97%)   | 0 / 44 (0.00%)   | 0 / 9 (0.00%)  |
| occurrences (all)                                | 1                 | 0                | 0              |
| Detachment of macular retinal pigment epithelium |                   |                  |                |
| subjects affected / exposed                      | 0 / 103 (0.00%)   | 0 / 44 (0.00%)   | 0 / 9 (0.00%)  |
| occurrences (all)                                | 0                 | 0                | 0              |
| Dry eye  |                   |                  |                |
| subjects affected / exposed                      | 21 / 103 (20.39%) | 7 / 44 (15.91%)  | 4 / 9 (44.44%) |
| occurrences (all)                                | 27                | 7                | 4              |
| Eye disorder                                     |                   |                  |                |
| subjects affected / exposed                      | 0 / 103 (0.00%)   | 0 / 44 (0.00%)   | 0 / 9 (0.00%)  |
| occurrences (all)                                | 0                 | 0                | 0              |
| Eye haematoma                                    |                   |                  |                |

|                             |                 |                |                |
|-----------------------------|-----------------|----------------|----------------|
| subjects affected / exposed | 0 / 103 (0.00%) | 0 / 44 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)           | 0               | 0              | 0              |
| Eye pain                    |                 |                |                |
| subjects affected / exposed | 1 / 103 (0.97%) | 0 / 44 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all)           | 1               | 0              | 1              |
| Eyelid pain                 |                 |                |                |
| subjects affected / exposed | 0 / 103 (0.00%) | 0 / 44 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all)           | 0               | 0              | 1              |
| Glaucoma                    |                 |                |                |
| subjects affected / exposed | 0 / 103 (0.00%) | 0 / 44 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all)           | 0               | 0              | 1              |
| Keratitis                   |                 |                |                |
| subjects affected / exposed | 4 / 103 (3.88%) | 1 / 44 (2.27%) | 2 / 9 (22.22%) |
| occurrences (all)           | 4               | 1              | 2              |
| Lacrimation increased       |                 |                |                |
| subjects affected / exposed | 2 / 103 (1.94%) | 1 / 44 (2.27%) | 1 / 9 (11.11%) |
| occurrences (all)           | 3               | 1              | 1              |
| Meibomian gland dysfunction |                 |                |                |
| subjects affected / exposed | 2 / 103 (1.94%) | 0 / 44 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all)           | 2               | 0              | 1              |
| Punctate keratitis          |                 |                |                |
| subjects affected / exposed | 2 / 103 (1.94%) | 1 / 44 (2.27%) | 1 / 9 (11.11%) |
| occurrences (all)           | 2               | 1              | 1              |
| Retinal detachment          |                 |                |                |
| subjects affected / exposed | 2 / 103 (1.94%) | 0 / 44 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)           | 2               | 0              | 0              |
| Subretinal fluid            |                 |                |                |
| subjects affected / exposed | 3 / 103 (2.91%) | 0 / 44 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all)           | 3               | 0              | 1              |
| Trichiasis                  |                 |                |                |
| subjects affected / exposed | 6 / 103 (5.83%) | 0 / 44 (0.00%) | 0 / 9 (0.00%)  |
| occurrences (all)           | 6               | 0              | 0              |
| Trichomegaly                |                 |                |                |
| subjects affected / exposed | 4 / 103 (3.88%) | 0 / 44 (0.00%) | 1 / 9 (11.11%) |
| occurrences (all)           | 4               | 0              | 1              |
| Vision blurred              |                 |                |                |

|   |                         |                        |                     |
|---|-------------------------|------------------------|---------------------|
| subjects affected / exposed<br>occurrences (all)                          | 6 / 103 (5.83%)<br>7    | 1 / 44 (2.27%)<br>3    | 1 / 9 (11.11%)<br>1 |
| Visual acuity reduced<br>subjects affected / exposed<br>occurrences (all) | 5 / 103 (4.85%)<br>5    | 0 / 44 (0.00%)<br>0    | 0 / 9 (0.00%)<br>0  |
| Visual impairment<br>subjects affected / exposed<br>occurrences (all)     | 3 / 103 (2.91%)<br>3    | 0 / 44 (0.00%)<br>0    | 0 / 9 (0.00%)<br>0  |
| Gastrointestinal disorders  |                         |                        |                     |
| Abdominal pain upper<br>subjects affected / exposed<br>occurrences (all)  | 5 / 103 (4.85%)<br>5    | 3 / 44 (6.82%)<br>4    | 0 / 9 (0.00%)<br>0  |
| Abdominal pain<br>subjects affected / exposed<br>occurrences (all)        | 20 / 103 (19.42%)<br>28 | 11 / 44 (25.00%)<br>12 | 1 / 9 (11.11%)<br>1 |
| Aphthous ulcer<br>subjects affected / exposed<br>occurrences (all)        | 1 / 103 (0.97%)<br>1    | 0 / 44 (0.00%)<br>0    | 1 / 9 (11.11%)<br>1 |
| Chapped lips<br>subjects affected / exposed<br>occurrences (all)          | 0 / 103 (0.00%)<br>0    | 0 / 44 (0.00%)<br>0    | 1 / 9 (11.11%)<br>1 |
| Constipation<br>subjects affected / exposed<br>occurrences (all)          | 36 / 103 (34.95%)<br>46 | 11 / 44 (25.00%)<br>13 | 4 / 9 (44.44%)<br>4 |
| Diarrhoea<br>subjects affected / exposed<br>occurrences (all)             | 53 / 103 (51.46%)<br>89 | 19 / 44 (43.18%)<br>28 | 6 / 9 (66.67%)<br>8 |
| Dry mouth<br>subjects affected / exposed<br>occurrences (all)             | 33 / 103 (32.04%)<br>35 | 13 / 44 (29.55%)<br>13 | 7 / 9 (77.78%)<br>7 |
| Dyspepsia<br>subjects affected / exposed<br>occurrences (all)             | 10 / 103 (9.71%)<br>16  | 1 / 44 (2.27%)<br>1    | 2 / 9 (22.22%)<br>2 |
| Dysphagia<br>subjects affected / exposed<br>occurrences (all)             | 4 / 103 (3.88%)<br>5    | 3 / 44 (6.82%)<br>3    | 0 / 9 (0.00%)<br>0  |

|  |                         |                        |                     |
|--|-------------------------|------------------------|---------------------|
| Gastrooesophageal reflux disease<br>subjects affected / exposed<br>occurrences (all) | 3 / 103 (2.91%)<br>3    | 0 / 44 (0.00%)<br>0    | 0 / 9 (0.00%)<br>0  |
| Gastrointestinal disorder<br>subjects affected / exposed<br>occurrences (all)        | 0 / 103 (0.00%)<br>0    | 0 / 44 (0.00%)<br>0    | 1 / 9 (11.11%)<br>1 |
| Haemorrhoids<br>subjects affected / exposed<br>occurrences (all)                     | 2 / 103 (1.94%)<br>2    | 0 / 44 (0.00%)<br>0    | 1 / 9 (11.11%)<br>1 |
| Glossodynia<br>subjects affected / exposed<br>occurrences (all)                      | 1 / 103 (0.97%)<br>1    | 1 / 44 (2.27%)<br>1    | 1 / 9 (11.11%)<br>1 |
| Lip pain<br>subjects affected / exposed<br>occurrences (all)                         | 0 / 103 (0.00%)<br>0    | 2 / 44 (4.55%)<br>4    | 1 / 9 (11.11%)<br>1 |
| Mouth ulceration<br>subjects affected / exposed<br>occurrences (all)                 | 2 / 103 (1.94%)<br>2    | 4 / 44 (9.09%)<br>4    | 0 / 9 (0.00%)<br>0  |
| Nausea<br>subjects affected / exposed<br>occurrences (all)                           | 28 / 103 (27.18%)<br>39 | 13 / 44 (29.55%)<br>17 | 1 / 9 (11.11%)<br>1 |
| Oral pain<br>subjects affected / exposed<br>occurrences (all)                        | 5 / 103 (4.85%)<br>5    | 4 / 44 (9.09%)<br>5    | 1 / 9 (11.11%)<br>1 |
| Stomatitis<br>subjects affected / exposed<br>occurrences (all)                       | 48 / 103 (46.60%)<br>70 | 13 / 44 (29.55%)<br>14 | 3 / 9 (33.33%)<br>3 |
| Tooth disorder<br>subjects affected / exposed<br>occurrences (all)                   | 0 / 103 (0.00%)<br>0    | 0 / 44 (0.00%)<br>0    | 0 / 9 (0.00%)<br>0  |
| Vomiting<br>subjects affected / exposed<br>occurrences (all)                         | 19 / 103 (18.45%)<br>29 | 10 / 44 (22.73%)<br>15 | 0 / 9 (0.00%)<br>0  |
| Skin and subcutaneous tissue disorders<br>Alopecia                                   |                         |                        |                     |

|   |                   |                  |                |
|---|-------------------|------------------|----------------|
| subjects affected / exposed                 | 49 / 103 (47.57%) | 16 / 44 (36.36%) | 7 / 9 (77.78%) |
| occurrences (all)                           | 50                | 16               | 7              |
| Dry skin                                    |                   |                  |                |
| subjects affected / exposed                 | 21 / 103 (20.39%) | 6 / 44 (13.64%)  | 4 / 9 (44.44%) |
| occurrences (all)                           | 23                | 6                | 5              |
| Erythema                                    |                   |                  |                |
| subjects affected / exposed                 | 3 / 103 (2.91%)   | 0 / 44 (0.00%)   | 1 / 9 (11.11%) |
| occurrences (all)                           | 3                 | 0                | 1              |
| Madarosis                                   |                   |                  |                |
| subjects affected / exposed                 | 3 / 103 (2.91%)   | 3 / 44 (6.82%)   | 0 / 9 (0.00%)  |
| occurrences (all)                           | 3                 | 3                | 0              |
| Nail disorder                               |                   |                  |                |
| subjects affected / exposed                 | 8 / 103 (7.77%)   | 2 / 44 (4.55%)   | 0 / 9 (0.00%)  |
| occurrences (all)                           | 9                 | 2                | 0              |
| Nail discolouration                         |                   |                  |                |
| subjects affected / exposed                 | 6 / 103 (5.83%)   | 5 / 44 (11.36%)  | 1 / 9 (11.11%) |
| occurrences (all)                           | 6                 | 5                | 1              |
| Nail toxicity                               |                   |                  |                |
| subjects affected / exposed                 | 5 / 103 (4.85%)   | 1 / 44 (2.27%)   | 0 / 9 (0.00%)  |
| occurrences (all)                           | 6                 | 1                | 0              |
| Nail dystrophy                              |                   |                  |                |
| subjects affected / exposed                 | 7 / 103 (6.80%)   | 2 / 44 (4.55%)   | 1 / 9 (11.11%) |
| occurrences (all)                           | 8                 | 2                | 1              |
| Onychalgia                                  |                   |                  |                |
| subjects affected / exposed                 | 4 / 103 (3.88%)   | 2 / 44 (4.55%)   | 0 / 9 (0.00%)  |
| occurrences (all)                           | 6                 | 2                | 0              |
| Onychomadesis                               |                   |                  |                |
| subjects affected / exposed                 | 6 / 103 (5.83%)   | 3 / 44 (6.82%)   | 1 / 9 (11.11%) |
| occurrences (all)                           | 7                 | 3                | 1              |
| Onycholysis                                 |                   |                  |                |
| subjects affected / exposed                 | 10 / 103 (9.71%)  | 6 / 44 (13.64%)  | 0 / 9 (0.00%)  |
| occurrences (all)                           | 10                | 7                | 0              |
| Palmar-plantar erythrodysaesthesia syndrome |                   |                  |                |
| subjects affected / exposed                 | 8 / 103 (7.77%)   | 3 / 44 (6.82%)   | 1 / 9 (11.11%) |
| occurrences (all)                           | 10                | 3                | 1              |

|   |                   |                 |                |
|---|-------------------|-----------------|----------------|
| Pruritus  |                   |                 |                |
| subjects affected / exposed                     | 9 / 103 (8.74%)   | 2 / 44 (4.55%)  | 0 / 9 (0.00%)  |
| occurrences (all)                               | 9                 | 2               | 0              |
| Rash  |                   |                 |                |
| subjects affected / exposed                     | 8 / 103 (7.77%)   | 2 / 44 (4.55%)  | 0 / 9 (0.00%)  |
| occurrences (all)                               | 8                 | 2               | 0              |
| Renal and urinary disorders                     |                   |                 |                |
| Acute kidney injury                             |                   |                 |                |
| subjects affected / exposed                     | 4 / 103 (3.88%)   | 5 / 44 (11.36%) | 1 / 9 (11.11%) |
| occurrences (all)                               | 4                 | 6               | 1              |
| Dysuria   |                   |                 |                |
| subjects affected / exposed                     | 4 / 103 (3.88%)   | 1 / 44 (2.27%)  | 1 / 9 (11.11%) |
| occurrences (all)                               | 5                 | 1               | 1              |
| Haematuria                                      |                   |                 |                |
| subjects affected / exposed                     | 8 / 103 (7.77%)   | 6 / 44 (13.64%) | 2 / 9 (22.22%) |
| occurrences (all)                               | 11                | 7               | 2              |
| Proteinuria                                     |                   |                 |                |
| subjects affected / exposed                     | 6 / 103 (5.83%)   | 2 / 44 (4.55%)  | 1 / 9 (11.11%) |
| occurrences (all)                               | 6                 | 2               | 1              |
| Endocrine disorders                             |                   |                 |                |
| Hypothyroidism                                  |                   |                 |                |
| subjects affected / exposed                     | 0 / 103 (0.00%)   | 0 / 44 (0.00%)  | 0 / 9 (0.00%)  |
| occurrences (all)                               | 0                 | 0               | 0              |
| Musculoskeletal and connective tissue disorders |                   |                 |                |
| Arthralgia                                      |                   |                 |                |
| subjects affected / exposed                     | 19 / 103 (18.45%) | 6 / 44 (13.64%) | 1 / 9 (11.11%) |
| occurrences (all)                               | 22                | 7               | 1              |
| Back pain                                       |                   |                 |                |
| subjects affected / exposed                     | 18 / 103 (17.48%) | 6 / 44 (13.64%) | 2 / 9 (22.22%) |
| occurrences (all)                               | 22                | 6               | 2              |
| Muscle fatigue                                  |                   |                 |                |
| subjects affected / exposed                     | 0 / 103 (0.00%)   | 0 / 44 (0.00%)  | 1 / 9 (11.11%) |
| occurrences (all)                               | 0                 | 0               | 1              |
| Muscle spasms                                   |                   |                 |                |
| subjects affected / exposed                     | 5 / 103 (4.85%)   | 1 / 44 (2.27%)  | 1 / 9 (11.11%) |
| occurrences (all)                               | 6                 | 1               | 1              |

|  |                         |                     |                     |
|--|-------------------------|---------------------|---------------------|
| Muscular weakness<br>subjects affected / exposed<br>occurrences (all)          | 9 / 103 (8.74%)<br>11   | 0 / 44 (0.00%)<br>0 | 1 / 9 (11.11%)<br>1 |
| Musculoskeletal chest pain<br>subjects affected / exposed<br>occurrences (all) | 0 / 103 (0.00%)<br>0    | 0 / 44 (0.00%)<br>0 | 1 / 9 (11.11%)<br>1 |
| Myalgia<br>subjects affected / exposed<br>occurrences (all)                    | 6 / 103 (5.83%)<br>8    | 1 / 44 (2.27%)<br>1 | 2 / 9 (22.22%)<br>2 |
| Neck pain<br>subjects affected / exposed<br>occurrences (all)                  | 5 / 103 (4.85%)<br>5    | 2 / 44 (4.55%)<br>2 | 1 / 9 (11.11%)<br>1 |
| Pain in extremity<br>subjects affected / exposed<br>occurrences (all)          | 12 / 103 (11.65%)<br>14 | 4 / 44 (9.09%)<br>5 | 1 / 9 (11.11%)<br>1 |
| Infections and infestations  |                         |                     |                     |
| Candida infection<br>subjects affected / exposed<br>occurrences (all)          | 1 / 103 (0.97%)<br>1    | 0 / 44 (0.00%)<br>0 | 1 / 9 (11.11%)<br>1 |
| Conjunctivitis<br>subjects affected / exposed<br>occurrences (all)             | 4 / 103 (3.88%)<br>5    | 2 / 44 (4.55%)<br>2 | 1 / 9 (11.11%)<br>1 |
| Conjunctivitis bacterial<br>subjects affected / exposed<br>occurrences (all)   | 0 / 103 (0.00%)<br>0    | 0 / 44 (0.00%)<br>0 | 1 / 9 (11.11%)<br>1 |
| Gingivitis<br>subjects affected / exposed<br>occurrences (all)                 | 2 / 103 (1.94%)<br>2    | 0 / 44 (0.00%)<br>0 | 1 / 9 (11.11%)<br>1 |
| Influenza<br>subjects affected / exposed<br>occurrences (all)                  | 0 / 103 (0.00%)<br>0    | 2 / 44 (4.55%)<br>2 | 0 / 9 (0.00%)<br>0  |
| Oral candidiasis<br>subjects affected / exposed<br>occurrences (all)           | 3 / 103 (2.91%)<br>4    | 1 / 44 (2.27%)<br>1 | 1 / 9 (11.11%)<br>1 |
| Oral herpes  |                         |                     |                     |



|   |                         |                        |                     |
|---|-------------------------|------------------------|---------------------|
| subjects affected / exposed<br>occurrences (all)                            | 0 / 103 (0.00%)<br>0    | 0 / 44 (0.00%)<br>0    | 1 / 9 (11.11%)<br>1 |
| Paronychia<br>subjects affected / exposed<br>occurrences (all)              | 3 / 103 (2.91%)<br>3    | 1 / 44 (2.27%)<br>1    | 0 / 9 (0.00%)<br>0  |
| Urinary tract infection<br>subjects affected / exposed<br>occurrences (all) | 25 / 103 (24.27%)<br>31 | 10 / 44 (22.73%)<br>16 | 1 / 9 (11.11%)<br>1 |
| Metabolism and nutrition disorders  |                         |                        |                     |
| Decreased appetite<br>subjects affected / exposed<br>occurrences (all)      | 32 / 103 (31.07%)<br>38 | 11 / 44 (25.00%)<br>12 | 4 / 9 (44.44%)<br>4 |
| Dehydration<br>subjects affected / exposed<br>occurrences (all)             | 8 / 103 (7.77%)<br>12   | 2 / 44 (4.55%)<br>2    | 1 / 9 (11.11%)<br>1 |
| Hypercalcaemia<br>subjects affected / exposed<br>occurrences (all)          | 11 / 103 (10.68%)<br>12 | 1 / 44 (2.27%)<br>2    | 1 / 9 (11.11%)<br>1 |
| Hypercreatininaemia<br>subjects affected / exposed<br>occurrences (all)     | 1 / 103 (0.97%)<br>1    | 0 / 44 (0.00%)<br>0    | 0 / 9 (0.00%)<br>0  |
| Hyperglycaemia<br>subjects affected / exposed<br>occurrences (all)          | 3 / 103 (2.91%)<br>3    | 3 / 44 (6.82%)<br>3    | 1 / 9 (11.11%)<br>1 |
| Hyperkalaemia<br>subjects affected / exposed<br>occurrences (all)           | 6 / 103 (5.83%)<br>7    | 4 / 44 (9.09%)<br>7    | 0 / 9 (0.00%)<br>0  |
| Hyperphosphataemia<br>subjects affected / exposed<br>occurrences (all)      | 35 / 103 (33.98%)<br>39 | 13 / 44 (29.55%)<br>15 | 4 / 9 (44.44%)<br>4 |
| Hypertriglyceridaemia<br>subjects affected / exposed<br>occurrences (all)   | 1 / 103 (0.97%)<br>1    | 0 / 44 (0.00%)<br>0    | 1 / 9 (11.11%)<br>1 |
| Hypomagnesaemia<br>subjects affected / exposed<br>occurrences (all)         | 3 / 103 (2.91%)<br>3    | 3 / 44 (6.82%)<br>3    | 1 / 9 (11.11%)<br>1 |

|  |                         |                       |                     |
|--|-------------------------|-----------------------|---------------------|
| Hypoalbuminaemia<br>subjects affected / exposed<br>occurrences (all)     | 8 / 103 (7.77%)<br>8    | 4 / 44 (9.09%)<br>4   | 0 / 9 (0.00%)<br>0  |
| Hyponatraemia<br>subjects affected / exposed<br>occurrences (all)        | 7 / 103 (6.80%)<br>9    | 6 / 44 (13.64%)<br>10 | 1 / 9 (11.11%)<br>1 |
| Hypophosphataemia<br>subjects affected / exposed<br>occurrences (all)    | 13 / 103 (12.62%)<br>20 | 3 / 44 (6.82%)<br>4   | 1 / 9 (11.11%)<br>2 |
| Hypouricaemia<br>subjects affected / exposed<br>occurrences (all)        | 0 / 103 (0.00%)<br>0    | 0 / 44 (0.00%)<br>0   | 0 / 9 (0.00%)<br>0  |
| Vitamin D deficiency<br>subjects affected / exposed<br>occurrences (all) | 4 / 103 (3.88%)<br>5    | 1 / 44 (2.27%)<br>1   | 1 / 9 (11.11%)<br>1 |

| <b>Non-serious adverse events</b>  | Cohort A-CD: FGFR3 mutations or fusions | Other-CD           |  |
|--|---|--------------------|--|
| Total subjects affected by non-serious adverse events<br>subjects affected / exposed | 99 / 101 (98.02%)                       | 3 / 3 (100.00%)    |  |
| Vascular disorders   |   |                    |  |
| Hypotension<br>subjects affected / exposed<br>occurrences (all)                      | 2 / 101 (1.98%)<br>2                    | 0 / 3 (0.00%)<br>0 |  |
| Orthostatic hypotension<br>subjects affected / exposed<br>occurrences (all)          | 0 / 101 (0.00%)<br>0                    | 0 / 3 (0.00%)<br>0 |  |
| General disorders and administration site conditions                                 |   |                    |  |
| Asthenia<br>subjects affected / exposed<br>occurrences (all)                         | 32 / 101 (31.68%)<br>37                 | 0 / 3 (0.00%)<br>0 |  |
| Chills<br>subjects affected / exposed<br>occurrences (all)                           | 2 / 101 (1.98%)<br>2                    | 0 / 3 (0.00%)<br>0 |  |
| Chest pain<br>subjects affected / exposed<br>occurrences (all)                       | 0 / 101 (0.00%)<br>0                    | 0 / 3 (0.00%)<br>0 |  |

|   |                   |                |  |
|---|-------------------|----------------|--|
| Fatigue   |                   |                |  |
| subjects affected / exposed                     | 29 / 101 (28.71%) | 1 / 3 (33.33%) |  |
| occurrences (all)                               | 33                | 1              |  |
| Influenza like illness                          |                   |                |  |
| subjects affected / exposed                     | 1 / 101 (0.99%)   | 0 / 3 (0.00%)  |  |
| occurrences (all)                               | 1                 | 0              |  |
| Mucosal inflammation                            |                   |                |  |
| subjects affected / exposed                     | 2 / 101 (1.98%)   | 0 / 3 (0.00%)  |  |
| occurrences (all)                               | 2                 | 0              |  |
| Oedema peripheral                               |                   |                |  |
| subjects affected / exposed                     | 10 / 101 (9.90%)  | 0 / 3 (0.00%)  |  |
| occurrences (all)                               | 10                | 0              |  |
| Pain  |                   |                |  |
| subjects affected / exposed                     | 3 / 101 (2.97%)   | 0 / 3 (0.00%)  |  |
| occurrences (all)                               | 3                 | 0              |  |
| Pyrexia   |                   |                |  |
| subjects affected / exposed                     | 12 / 101 (11.88%) | 0 / 3 (0.00%)  |  |
| occurrences (all)                               | 17                | 0              |  |
| Reproductive system and breast disorders        |                   |                |  |
| Pelvic pain                                     |                   |                |  |
| subjects affected / exposed                     | 2 / 101 (1.98%)   | 0 / 3 (0.00%)  |  |
| occurrences (all)                               | 2                 | 0              |  |
| Respiratory, thoracic and mediastinal disorders |                   |                |  |
| Cough   |                   |                |  |
| subjects affected / exposed                     | 5 / 101 (4.95%)   | 1 / 3 (33.33%) |  |
| occurrences (all)                               | 5                 | 1              |  |
| Dyspnoea  |                   |                |  |
| subjects affected / exposed                     | 5 / 101 (4.95%)   | 1 / 3 (33.33%) |  |
| occurrences (all)                               | 5                 | 1              |  |
| Dysphonia                                       |                   |                |  |
| subjects affected / exposed                     | 4 / 101 (3.96%)   | 0 / 3 (0.00%)  |  |
| occurrences (all)                               | 4                 | 0              |  |
| Epistaxis                                       |                   |                |  |
| subjects affected / exposed                     | 14 / 101 (13.86%) | 0 / 3 (0.00%)  |  |
| occurrences (all)                               | 18                | 0              |  |
| Nasal dryness                                   |                   |                |  |

|                                      |                   |                |  |
|--------------------------------------|-------------------|----------------|--|
| subjects affected / exposed          | 5 / 101 (4.95%)   | 0 / 3 (0.00%)  |  |
| occurrences (all)                    | 5                 | 0              |  |
| Oropharyngeal pain                   |                   |                |  |
| subjects affected / exposed          | 5 / 101 (4.95%)   | 0 / 3 (0.00%)  |  |
| occurrences (all)                    | 5                 | 0              |  |
| Upper-airway cough syndrome          |                   |                |  |
| subjects affected / exposed          | 0 / 101 (0.00%)   | 1 / 3 (33.33%) |  |
| occurrences (all)                    | 0                 | 1              |  |
| Psychiatric disorders                |                   |                |  |
| Anxiety                              |                   |                |  |
| subjects affected / exposed          | 1 / 101 (0.99%)   | 0 / 3 (0.00%)  |  |
| occurrences (all)                    | 1                 | 0              |  |
| Insomnia                             |                   |                |  |
| subjects affected / exposed          | 5 / 101 (4.95%)   | 0 / 3 (0.00%)  |  |
| occurrences (all)                    | 5                 | 0              |  |
| Investigations                       |                   |                |  |
| Alanine aminotransferase increased   |                   |                |  |
| subjects affected / exposed          | 9 / 101 (8.91%)   | 0 / 3 (0.00%)  |  |
| occurrences (all)                    | 11                | 0              |  |
| Aspartate aminotransferase increased |                   |                |  |
| subjects affected / exposed          | 7 / 101 (6.93%)   | 0 / 3 (0.00%)  |  |
| occurrences (all)                    | 8                 | 0              |  |
| Blood creatinine increased           |                   |                |  |
| subjects affected / exposed          | 20 / 101 (19.80%) | 1 / 3 (33.33%) |  |
| occurrences (all)                    | 22                | 1              |  |
| Blood phosphorus increased           |                   |                |  |
| subjects affected / exposed          | 13 / 101 (12.87%) | 1 / 3 (33.33%) |  |
| occurrences (all)                    | 23                | 1              |  |
| Lymphocyte count decreased           |                   |                |  |
| subjects affected / exposed          | 1 / 101 (0.99%)   | 0 / 3 (0.00%)  |  |
| occurrences (all)                    | 1                 | 0              |  |
| Vitamin D decreased                  |                   |                |  |
| subjects affected / exposed          | 2 / 101 (1.98%)   | 0 / 3 (0.00%)  |  |
| occurrences (all)                    | 2                 | 0              |  |
| Weight decreased                     |                   |                |  |

|  |                         |                    |  |
|--|-------------------------|--------------------|--|
| subjects affected / exposed<br>occurrences (all) | 12 / 101 (11.88%)<br>12 | 0 / 3 (0.00%)<br>0 |  |
| Injury, poisoning and procedural complications   |                         |                    |  |
| Contusion  |                         |                    |  |
| subjects affected / exposed                      | 2 / 101 (1.98%)         | 1 / 3 (33.33%)     |  |
| occurrences (all)                                | 2                       | 1                  |  |
| Skin abrasion                                    |                         |                    |  |
| subjects affected / exposed                      | 1 / 101 (0.99%)         | 0 / 3 (0.00%)      |  |
| occurrences (all)                                | 1                       | 0                  |  |
| Cardiac disorders                                |                         |                    |  |
| Bundle branch block left                         |                         |                    |  |
| subjects affected / exposed                      | 0 / 101 (0.00%)         | 1 / 3 (33.33%)     |  |
| occurrences (all)                                | 0                       | 1                  |  |
| Nervous system disorders                         |                         |                    |  |
| Ageusia  |                         |                    |  |
| subjects affected / exposed                      | 3 / 101 (2.97%)         | 0 / 3 (0.00%)      |  |
| occurrences (all)                                | 4                       | 0                  |  |
| Cognitive disorder                               |                         |                    |  |
| subjects affected / exposed                      | 0 / 101 (0.00%)         | 0 / 3 (0.00%)      |  |
| occurrences (all)                                | 0                       | 0                  |  |
| Dizziness  |                         |                    |  |
| subjects affected / exposed                      | 4 / 101 (3.96%)         | 0 / 3 (0.00%)      |  |
| occurrences (all)                                | 6                       | 0                  |  |
| Disturbance in attention                         |                         |                    |  |
| subjects affected / exposed                      | 0 / 101 (0.00%)         | 0 / 3 (0.00%)      |  |
| occurrences (all)                                | 0                       | 0                  |  |
| Dysgeusia  |                         |                    |  |
| subjects affected / exposed                      | 31 / 101 (30.69%)       | 1 / 3 (33.33%)     |  |
| occurrences (all)                                | 33                      | 1                  |  |
| Headache   |                         |                    |  |
| subjects affected / exposed                      | 5 / 101 (4.95%)         | 0 / 3 (0.00%)      |  |
| occurrences (all)                                | 5                       | 0                  |  |
| Hypoaesthesia                                    |                         |                    |  |
| subjects affected / exposed                      | 1 / 101 (0.99%)         | 1 / 3 (33.33%)     |  |
| occurrences (all)                                | 1                       | 1                  |  |
| Lethargy   |                         |                    |  |

|  |                   |                |  |
|--|-------------------|----------------|--|
| subjects affected / exposed                      | 0 / 101 (0.00%)   | 0 / 3 (0.00%)  |  |
| occurrences (all)                                | 0                 | 0              |  |
| Neuropathy peripheral                            |                   |                |  |
| subjects affected / exposed                      | 1 / 101 (0.99%)   | 1 / 3 (33.33%) |  |
| occurrences (all)                                | 1                 | 1              |  |
| Peripheral sensory neuropathy                    |                   |                |  |
| subjects affected / exposed                      | 3 / 101 (2.97%)   | 0 / 3 (0.00%)  |  |
| occurrences (all)                                | 5                 | 0              |  |
| Transient ischaemic attack                       |                   |                |  |
| subjects affected / exposed                      | 0 / 101 (0.00%)   | 0 / 3 (0.00%)  |  |
| occurrences (all)                                | 0                 | 0              |  |
| Blood and lymphatic system disorders             |                   |                |  |
| Anaemia  |                   |                |  |
| subjects affected / exposed                      | 18 / 101 (17.82%) | 0 / 3 (0.00%)  |  |
| occurrences (all)                                | 19                | 0              |  |
| Iron deficiency anaemia                          |                   |                |  |
| subjects affected / exposed                      | 0 / 101 (0.00%)   | 1 / 3 (33.33%) |  |
| occurrences (all)                                | 0                 | 1              |  |
| Eye disorders                                    |                   |                |  |
| Arcus lipoides                                   |                   |                |  |
| subjects affected / exposed                      | 0 / 101 (0.00%)   | 1 / 3 (33.33%) |  |
| occurrences (all)                                | 0                 | 1              |  |
| Blepharitis                                      |                   |                |  |
| subjects affected / exposed                      | 9 / 101 (8.91%)   | 1 / 3 (33.33%) |  |
| occurrences (all)                                | 9                 | 1              |  |
| Cataract   |                   |                |  |
| subjects affected / exposed                      | 6 / 101 (5.94%)   | 0 / 3 (0.00%)  |  |
| occurrences (all)                                | 6                 | 0              |  |
| Corneal neovascularisation                       |                   |                |  |
| subjects affected / exposed                      | 0 / 101 (0.00%)   | 1 / 3 (33.33%) |  |
| occurrences (all)                                | 0                 | 1              |  |
| Detachment of macular retinal pigment epithelium |                   |                |  |
| subjects affected / exposed                      | 0 / 101 (0.00%)   | 1 / 3 (33.33%) |  |
| occurrences (all)                                | 0                 | 1              |  |
| Dry eye  |                   |                |  |

|                             |                   |                |
|-----------------------------|-------------------|----------------|
| subjects affected / exposed | 19 / 101 (18.81%) | 1 / 3 (33.33%) |
| occurrences (all)           | 20                | 1              |
| Eye disorder                |                   |                |
| subjects affected / exposed | 0 / 101 (0.00%)   | 1 / 3 (33.33%) |
| occurrences (all)           | 0                 | 1              |
| Eye haematoma               |                   |                |
| subjects affected / exposed | 1 / 101 (0.99%)   | 1 / 3 (33.33%) |
| occurrences (all)           | 1                 | 1              |
| Eye pain                    |                   |                |
| subjects affected / exposed | 2 / 101 (1.98%)   | 0 / 3 (0.00%)  |
| occurrences (all)           | 4                 | 0              |
| Eyelid pain                 |                   |                |
| subjects affected / exposed | 0 / 101 (0.00%)   | 0 / 3 (0.00%)  |
| occurrences (all)           | 0                 | 0              |
| Glaucoma                    |                   |                |
| subjects affected / exposed | 0 / 101 (0.00%)   | 0 / 3 (0.00%)  |
| occurrences (all)           | 0                 | 0              |
| Keratitis                   |                   |                |
| subjects affected / exposed | 5 / 101 (4.95%)   | 0 / 3 (0.00%)  |
| occurrences (all)           | 5                 | 0              |
| Lacrimation increased       |                   |                |
| subjects affected / exposed | 3 / 101 (2.97%)   | 0 / 3 (0.00%)  |
| occurrences (all)           | 3                 | 0              |
| Meibomian gland dysfunction |                   |                |
| subjects affected / exposed | 0 / 101 (0.00%)   | 0 / 3 (0.00%)  |
| occurrences (all)           | 0                 | 0              |
| Punctate keratitis          |                   |                |
| subjects affected / exposed | 7 / 101 (6.93%)   | 0 / 3 (0.00%)  |
| occurrences (all)           | 8                 | 0              |
| Retinal detachment          |                   |                |
| subjects affected / exposed | 9 / 101 (8.91%)   | 1 / 3 (33.33%) |
| occurrences (all)           | 9                 | 1              |
| Subretinal fluid            |                   |                |
| subjects affected / exposed | 0 / 101 (0.00%)   | 0 / 3 (0.00%)  |
| occurrences (all)           | 0                 | 0              |
| Trichiasis                  |                   |                |

|                             |                   |                |  |
|-----------------------------|-------------------|----------------|--|
| subjects affected / exposed | 5 / 101 (4.95%)   | 0 / 3 (0.00%)  |  |
| occurrences (all)           | 6                 | 0              |  |
| Trichomegaly                |                   |                |  |
| subjects affected / exposed | 1 / 101 (0.99%)   | 0 / 3 (0.00%)  |  |
| occurrences (all)           | 1                 | 0              |  |
| Vision blurred              |                   |                |  |
| subjects affected / exposed | 7 / 101 (6.93%)   | 0 / 3 (0.00%)  |  |
| occurrences (all)           | 8                 | 0              |  |
| Visual acuity reduced       |                   |                |  |
| subjects affected / exposed | 10 / 101 (9.90%)  | 0 / 3 (0.00%)  |  |
| occurrences (all)           | 10                | 0              |  |
| Visual impairment           |                   |                |  |
| subjects affected / exposed | 6 / 101 (5.94%)   | 0 / 3 (0.00%)  |  |
| occurrences (all)           | 6                 | 0              |  |
| Gastrointestinal disorders  |                   |                |  |
| Abdominal pain upper        |                   |                |  |
| subjects affected / exposed | 6 / 101 (5.94%)   | 0 / 3 (0.00%)  |  |
| occurrences (all)           | 7                 | 0              |  |
| Abdominal pain              |                   |                |  |
| subjects affected / exposed | 7 / 101 (6.93%)   | 2 / 3 (66.67%) |  |
| occurrences (all)           | 9                 | 2              |  |
| Aphthous ulcer              |                   |                |  |
| subjects affected / exposed | 0 / 101 (0.00%)   | 0 / 3 (0.00%)  |  |
| occurrences (all)           | 0                 | 0              |  |
| Chapped lips                |                   |                |  |
| subjects affected / exposed | 0 / 101 (0.00%)   | 0 / 3 (0.00%)  |  |
| occurrences (all)           | 0                 | 0              |  |
| Constipation                |                   |                |  |
| subjects affected / exposed | 33 / 101 (32.67%) | 1 / 3 (33.33%) |  |
| occurrences (all)           | 35                | 1              |  |
| Diarrhoea                   |                   |                |  |
| subjects affected / exposed | 34 / 101 (33.66%) | 2 / 3 (66.67%) |  |
| occurrences (all)           | 55                | 2              |  |
| Dry mouth                   |                   |                |  |
| subjects affected / exposed | 39 / 101 (38.61%) | 1 / 3 (33.33%) |  |
| occurrences (all)           | 39                | 1              |  |



|                                  |                   |                |
|----------------------------------|-------------------|----------------|
| Dyspepsia                        |                   |                |
| subjects affected / exposed      | 7 / 101 (6.93%)   | 0 / 3 (0.00%)  |
| occurrences (all)                | 7                 | 0              |
| Dysphagia                        |                   |                |
| subjects affected / exposed      | 2 / 101 (1.98%)   | 1 / 3 (33.33%) |
| occurrences (all)                | 2                 | 1              |
| Gastrooesophageal reflux disease |                   |                |
| subjects affected / exposed      | 7 / 101 (6.93%)   | 0 / 3 (0.00%)  |
| occurrences (all)                | 7                 | 0              |
| Gastrointestinal disorder        |                   |                |
| subjects affected / exposed      | 0 / 101 (0.00%)   | 0 / 3 (0.00%)  |
| occurrences (all)                | 0                 | 0              |
| Haemorrhoids                     |                   |                |
| subjects affected / exposed      | 2 / 101 (1.98%)   | 0 / 3 (0.00%)  |
| occurrences (all)                | 2                 | 0              |
| Glossodynia                      |                   |                |
| subjects affected / exposed      | 1 / 101 (0.99%)   | 0 / 3 (0.00%)  |
| occurrences (all)                | 1                 | 0              |
| Lip pain                         |                   |                |
| subjects affected / exposed      | 0 / 101 (0.00%)   | 0 / 3 (0.00%)  |
| occurrences (all)                | 0                 | 0              |
| Mouth ulceration                 |                   |                |
| subjects affected / exposed      | 1 / 101 (0.99%)   | 0 / 3 (0.00%)  |
| occurrences (all)                | 1                 | 0              |
| Nausea                           |                   |                |
| subjects affected / exposed      | 18 / 101 (17.82%) | 0 / 3 (0.00%)  |
| occurrences (all)                | 19                | 0              |
| Oral pain                        |                   |                |
| subjects affected / exposed      | 1 / 101 (0.99%)   | 0 / 3 (0.00%)  |
| occurrences (all)                | 1                 | 0              |
| Stomatitis                       |                   |                |
| subjects affected / exposed      | 45 / 101 (44.55%) | 1 / 3 (33.33%) |
| occurrences (all)                | 56                | 1              |
| Tooth disorder                   |                   |                |
| subjects affected / exposed      | 1 / 101 (0.99%)   | 1 / 3 (33.33%) |
| occurrences (all)                | 1                 | 1              |

|  |                   |                |  |
|--|-------------------|----------------|--|
| Vomiting                               |                   |                |  |
| subjects affected / exposed            | 12 / 101 (11.88%) | 1 / 3 (33.33%) |  |
| occurrences (all)                      | 19                | 1              |  |
| Skin and subcutaneous tissue disorders |                   |                |  |
| Alopecia                               |                   |                |  |
| subjects affected / exposed            | 38 / 101 (37.62%) | 1 / 3 (33.33%) |  |
| occurrences (all)                      | 38                | 1              |  |
| Dry skin                               |                   |                |  |
| subjects affected / exposed            | 22 / 101 (21.78%) | 2 / 3 (66.67%) |  |
| occurrences (all)                      | 23                | 2              |  |
| Erythema                               |                   |                |  |
| subjects affected / exposed            | 2 / 101 (1.98%)   | 0 / 3 (0.00%)  |  |
| occurrences (all)                      | 3                 | 0              |  |
| Madarosis                              |                   |                |  |
| subjects affected / exposed            | 2 / 101 (1.98%)   | 0 / 3 (0.00%)  |  |
| occurrences (all)                      | 2                 | 0              |  |
| Nail disorder                          |                   |                |  |
| subjects affected / exposed            | 10 / 101 (9.90%)  | 0 / 3 (0.00%)  |  |
| occurrences (all)                      | 11                | 0              |  |
| Nail discolouration                    |                   |                |  |
| subjects affected / exposed            | 10 / 101 (9.90%)  | 1 / 3 (33.33%) |  |
| occurrences (all)                      | 10                | 1              |  |
| Nail toxicity                          |                   |                |  |
| subjects affected / exposed            | 7 / 101 (6.93%)   | 0 / 3 (0.00%)  |  |
| occurrences (all)                      | 7                 | 0              |  |
| Nail dystrophy                         |                   |                |  |
| subjects affected / exposed            | 6 / 101 (5.94%)   | 0 / 3 (0.00%)  |  |
| occurrences (all)                      | 6                 | 0              |  |
| Onychalgia                             |                   |                |  |
| subjects affected / exposed            | 6 / 101 (5.94%)   | 1 / 3 (33.33%) |  |
| occurrences (all)                      | 6                 | 1              |  |
| Onychomadesis                          |                   |                |  |
| subjects affected / exposed            | 8 / 101 (7.92%)   | 0 / 3 (0.00%)  |  |
| occurrences (all)                      | 8                 | 0              |  |
| Onycholysis                            |                   |                |  |

|   |                   |                |  |
|---|-------------------|----------------|--|
| subjects affected / exposed                     | 10 / 101 (9.90%)  | 1 / 3 (33.33%) |  |
| occurrences (all)                               | 10                | 1              |  |
| Palmar-plantar erythrodysaesthesia syndrome     |                   |                |  |
| subjects affected / exposed                     | 28 / 101 (27.72%) | 0 / 3 (0.00%)  |  |
| occurrences (all)                               | 31                | 0              |  |
| Pruritus  |                   |                |  |
| subjects affected / exposed                     | 4 / 101 (3.96%)   | 0 / 3 (0.00%)  |  |
| occurrences (all)                               | 4                 | 0              |  |
| Rash  |                   |                |  |
| subjects affected / exposed                     | 8 / 101 (7.92%)   | 0 / 3 (0.00%)  |  |
| occurrences (all)                               | 8                 | 0              |  |
| Renal and urinary disorders                     |                   |                |  |
| Acute kidney injury                             |                   |                |  |
| subjects affected / exposed                     | 4 / 101 (3.96%)   | 0 / 3 (0.00%)  |  |
| occurrences (all)                               | 4                 | 0              |  |
| Dysuria   |                   |                |  |
| subjects affected / exposed                     | 3 / 101 (2.97%)   | 0 / 3 (0.00%)  |  |
| occurrences (all)                               | 3                 | 0              |  |
| Haematuria                                      |                   |                |  |
| subjects affected / exposed                     | 12 / 101 (11.88%) | 0 / 3 (0.00%)  |  |
| occurrences (all)                               | 15                | 0              |  |
| Proteinuria                                     |                   |                |  |
| subjects affected / exposed                     | 0 / 101 (0.00%)   | 0 / 3 (0.00%)  |  |
| occurrences (all)                               | 0                 | 0              |  |
| Endocrine disorders                             |                   |                |  |
| Hypothyroidism                                  |                   |                |  |
| subjects affected / exposed                     | 0 / 101 (0.00%)   | 1 / 3 (33.33%) |  |
| occurrences (all)                               | 0                 | 1              |  |
| Musculoskeletal and connective tissue disorders |                   |                |  |
| Arthralgia                                      |                   |                |  |
| subjects affected / exposed                     | 19 / 101 (18.81%) | 0 / 3 (0.00%)  |  |
| occurrences (all)                               | 22                | 0              |  |
| Back pain                                       |                   |                |  |
| subjects affected / exposed                     | 15 / 101 (14.85%) | 1 / 3 (33.33%) |  |
| occurrences (all)                               | 15                | 1              |  |
| Muscle fatigue                                  |                   |                |  |

|                             |                   |                |  |
|-----------------------------|-------------------|----------------|--|
| subjects affected / exposed | 0 / 101 (0.00%)   | 0 / 3 (0.00%)  |  |
| occurrences (all)           | 0                 | 0              |  |
| Muscle spasms               |                   |                |  |
| subjects affected / exposed | 5 / 101 (4.95%)   | 1 / 3 (33.33%) |  |
| occurrences (all)           | 5                 | 1              |  |
| Muscular weakness           |                   |                |  |
| subjects affected / exposed | 4 / 101 (3.96%)   | 0 / 3 (0.00%)  |  |
| occurrences (all)           | 4                 | 0              |  |
| Musculoskeletal chest pain  |                   |                |  |
| subjects affected / exposed | 1 / 101 (0.99%)   | 0 / 3 (0.00%)  |  |
| occurrences (all)           | 1                 | 0              |  |
| Myalgia                     |                   |                |  |
| subjects affected / exposed | 1 / 101 (0.99%)   | 0 / 3 (0.00%)  |  |
| occurrences (all)           | 1                 | 0              |  |
| Neck pain                   |                   |                |  |
| subjects affected / exposed | 0 / 101 (0.00%)   | 0 / 3 (0.00%)  |  |
| occurrences (all)           | 0                 | 0              |  |
| Pain in extremity           |                   |                |  |
| subjects affected / exposed | 15 / 101 (14.85%) | 1 / 3 (33.33%) |  |
| occurrences (all)           | 18                | 1              |  |
| Infections and infestations |                   |                |  |
| Candida infection           |                   |                |  |
| subjects affected / exposed | 0 / 101 (0.00%)   | 0 / 3 (0.00%)  |  |
| occurrences (all)           | 0                 | 0              |  |
| Conjunctivitis              |                   |                |  |
| subjects affected / exposed | 6 / 101 (5.94%)   | 1 / 3 (33.33%) |  |
| occurrences (all)           | 6                 | 1              |  |
| Conjunctivitis bacterial    |                   |                |  |
| subjects affected / exposed | 0 / 101 (0.00%)   | 0 / 3 (0.00%)  |  |
| occurrences (all)           | 0                 | 0              |  |
| Gingivitis                  |                   |                |  |
| subjects affected / exposed | 0 / 101 (0.00%)   | 0 / 3 (0.00%)  |  |
| occurrences (all)           | 0                 | 0              |  |
| Influenza                   |                   |                |  |
| subjects affected / exposed | 0 / 101 (0.00%)   | 1 / 3 (33.33%) |  |
| occurrences (all)           | 0                 | 1              |  |

|                                    |                   |                |  |
|------------------------------------|-------------------|----------------|--|
| Oral candidiasis                   |                   |                |  |
| subjects affected / exposed        | 3 / 101 (2.97%)   | 0 / 3 (0.00%)  |  |
| occurrences (all)                  | 3                 | 0              |  |
| Oral herpes                        |                   |                |  |
| subjects affected / exposed        | 0 / 101 (0.00%)   | 0 / 3 (0.00%)  |  |
| occurrences (all)                  | 0                 | 0              |  |
| Paronychia                         |                   |                |  |
| subjects affected / exposed        | 8 / 101 (7.92%)   | 1 / 3 (33.33%) |  |
| occurrences (all)                  | 10                | 1              |  |
| Urinary tract infection            |                   |                |  |
| subjects affected / exposed        | 10 / 101 (9.90%)  | 0 / 3 (0.00%)  |  |
| occurrences (all)                  | 12                | 0              |  |
| Metabolism and nutrition disorders |                   |                |  |
| Decreased appetite                 |                   |                |  |
| subjects affected / exposed        | 29 / 101 (28.71%) | 0 / 3 (0.00%)  |  |
| occurrences (all)                  | 33                | 0              |  |
| Dehydration                        |                   |                |  |
| subjects affected / exposed        | 3 / 101 (2.97%)   | 0 / 3 (0.00%)  |  |
| occurrences (all)                  | 3                 | 0              |  |
| Hypercalcaemia                     |                   |                |  |
| subjects affected / exposed        | 7 / 101 (6.93%)   | 0 / 3 (0.00%)  |  |
| occurrences (all)                  | 8                 | 0              |  |
| Hypercreatininaemia                |                   |                |  |
| subjects affected / exposed        | 6 / 101 (5.94%)   | 0 / 3 (0.00%)  |  |
| occurrences (all)                  | 6                 | 0              |  |
| Hyperglycaemia                     |                   |                |  |
| subjects affected / exposed        | 1 / 101 (0.99%)   | 0 / 3 (0.00%)  |  |
| occurrences (all)                  | 1                 | 0              |  |
| Hyperkalaemia                      |                   |                |  |
| subjects affected / exposed        | 8 / 101 (7.92%)   | 0 / 3 (0.00%)  |  |
| occurrences (all)                  | 11                | 0              |  |
| Hyperphosphataemia                 |                   |                |  |
| subjects affected / exposed        | 56 / 101 (55.45%) | 2 / 3 (66.67%) |  |
| occurrences (all)                  | 95                | 2              |  |
| Hypertriglyceridaemia              |                   |                |  |

|                             |                 |                |  |
|-----------------------------|-----------------|----------------|--|
| subjects affected / exposed | 0 / 101 (0.00%) | 0 / 3 (0.00%)  |  |
| occurrences (all)           | 0               | 0              |  |
| Hypomagnesaemia             |                 |                |  |
| subjects affected / exposed | 2 / 101 (1.98%) | 1 / 3 (33.33%) |  |
| occurrences (all)           | 2               | 1              |  |
| Hypoalbuminaemia            |                 |                |  |
| subjects affected / exposed | 2 / 101 (1.98%) | 0 / 3 (0.00%)  |  |
| occurrences (all)           | 2               | 0              |  |
| Hyponatraemia               |                 |                |  |
| subjects affected / exposed | 9 / 101 (8.91%) | 0 / 3 (0.00%)  |  |
| occurrences (all)           | 12              | 0              |  |
| Hypophosphataemia           |                 |                |  |
| subjects affected / exposed | 4 / 101 (3.96%) | 0 / 3 (0.00%)  |  |
| occurrences (all)           | 4               | 0              |  |
| Hypouricaemia               |                 |                |  |
| subjects affected / exposed | 0 / 101 (0.00%) | 1 / 3 (33.33%) |  |
| occurrences (all)           | 0               | 1              |  |
| Vitamin D deficiency        |                 |                |  |
| subjects affected / exposed | 2 / 101 (1.98%) | 1 / 3 (33.33%) |  |
| occurrences (all)           | 2               | 2              |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date              | Amendment  |
|-------------------|--|
| 27 September 2016 | The primary purpose of this amendment was to update language based on Regulatory Agencies comments. Updates included but were not limited to clarification of inclusion and exclusion criteria, the addition of an independent data monitoring committee, and the removal of language indicating the futility analysis was nonbinding. |
| 17 November 2016  | The primary purpose of this amendment was to change the parameters associated with an exclusion criterion.   |
| 02 February 2017  | The primary purpose of this amendment was to revise language in the Protocol to provide flexibility for enrollment and to update previous clinical experience data to align with the Investigator's Brochure (version 3).  |
| 29 November 2017  | The primary purpose of this amendment was to refine the participant population, to divide the study population into cohorts, and to provide a list of possible eligible alterations.   |
| 18 June 2018      | The main purpose of this amendment was to add language to allow for continuous administration of pemigatinib. Updated clinical data were added to support continuous administration.<br>Additional language was added for Japanese participants. Other modifications were made based on new preclinical and/or clinical data.          |
| 20 November 2018  | The primary purpose of this amendment was to include up-titration language, to expand translational sciences assessments, and to include additional safety data.   |
| 09 March 2020     | The primary purpose of this amendment was to incorporate previous administrative changes and include updated language for comprehensive eye examination, per Food and Drug Administration (FDA) feedback.  |

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported