



## Clinical trial results:

### Non-Comparative, Open-Label, Multiple Cohort, Phase 1/2 Study of Nivolumab Monotherapy and Nivolumab Combination Therapy in Subjects with Virus-Positive and Virus-Negative Solid Tumors

#### Summary

|                          |                 |
|--------------------------|-----------------|
| EudraCT number           | 2015-000230-29  |
| Trial protocol           | NL DE BE GB ES  |
| Global end of trial date | 24 October 2022 |

#### Results information

|                                |                  |
|--------------------------------|------------------|
| Result version number          | v1 (current)     |
| This version publication date  | 01 November 2023 |
| First version publication date | 01 November 2023 |

#### Trial information

##### Trial identification

|                       |           |
|-----------------------|-----------|
| Sponsor protocol code | CA209-358 |
|-----------------------|-----------|

##### Additional study identifiers

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

Notes:

#### Sponsors

|                              |   |
|------------------------------|---|
| Sponsor organisation name    | Bristol-Myers Squibb  |
| Sponsor organisation address | Chaussée de la Hulpe 185, Brussels, Belgium, 1170   |
| Public contact               | EU Study Start-Up Unit, Bristol-Myers Squibb International Corporation, Clinical.Trials@bms.com |
| Scientific contact           | Bristol-Myers Squibb Study Director, Bristol-Myers Squibb, Clinical.Trials@bms.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                       | 28 November 2022 |
| Is this the analysis of the primary completion data? | No               |
| Global end of trial reached?                         | Yes              |
| Global end of trial date                             | 24 October 2022  |
| Was the trial ended prematurely?                     | No               |

Notes:

## General information about the trial

Main objective of the trial:

To investigate safety and efficacy of Nivolumab monotherapy and Nivolumab combination therapy in subjects with viral positive and viral negative multiple tumor types

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Conference on Harmonization Good Clinical Practice Guidelines. All the local regulatory requirements pertinent to safety of trial participants were followed.

Background therapy: -

Evidence for comparator: -

|   |                 |
|---|-----------------|
| Actual start date of recruitment                          | 13 October 2015 |
| Long term follow-up planned                               | No              |
| Independent data monitoring committee (IDMC) involvement? | No              |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |  |
|--------------------------------------|--|
| Country: Number of subjects enrolled | Belgium: 14                                |
| Country: Number of subjects enrolled | France: 52                                 |
| Country: Number of subjects enrolled | Germany: 20                                |
| Country: Number of subjects enrolled | Japan: 21                                  |
| Country: Number of subjects enrolled | Netherlands: 32                            |
| Country: Number of subjects enrolled | Korea, Democratic People's Republic of: 15 |
| Country: Number of subjects enrolled | Spain: 97                                  |
| Country: Number of subjects enrolled | United Kingdom: 55                         |
| Country: Number of subjects enrolled | United States: 239                         |
| Country: Number of subjects enrolled | Taiwan: 6                                  |
| Country: Number of subjects enrolled | Mexico: 27                                 |
| Worldwide total number of subjects   | 578  |
| EEA total number of subjects         | 215  |

Notes:

### Subjects enrolled per age group

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

|  |     |
|--|-----|
| wk                                       |     |
| Newborns (0-27 days)                     | 0   |
| Infants and toddlers (28 days-23 months) | 0   |
| Children (2-11 years)                    | 0   |
| Adolescents (12-17 years)                | 0   |
| Adults (18-64 years)                     | 400 |
| From 65 to 84 years                      | 170 |
| 85 years and over                        | 8   |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

578 participants treated

### Period 1

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

### Arms

|                              |     |
|------------------------------|-----|
| Are arms mutually exclusive? | Yes |
|------------------------------|-----|

|                  |                        |
|------------------|------------------------|
| <b>Arm title</b> | Metastatic Monotherapy |
|------------------|------------------------|

Arm description:

Nivolumab IV over 30 minutes at 240 mg every 2 weeks for a maximum of 24 months or until disease progression, unacceptable toxicity, or withdrawal of consent, whichever comes first

|  |                        |
|--|------------------------|
| Arm type                               | Experimental           |
| Investigational medicinal product name | Nivolumab              |
| Investigational medicinal product code | BMS-936558             |
| Other name                             |                        |
| Pharmaceutical forms                   | Solution for injection |
| Routes of administration               | Intravenous use        |

Dosage and administration details:

240 mg every 2 weeks for a maximum of 24 months

|                  |                    |
|------------------|--------------------|
| <b>Arm title</b> | Metastatic Combo A |
|------------------|--------------------|

Arm description:

Nivolumab 3 mg/kg IV over 30 minutes every 2 weeks + Ipilimumab 1 mg/kg IV over 30 minutes every 6 weeks for a maximum of 24 months or until disease progression, unacceptable toxicity, or withdrawal of consent, whichever comes first

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

Dosage and administration details:

1 mg/kg every 6 weeks for a maximum of 24 months

|  |                        |
|--|------------------------|
| Investigational medicinal product name | Nivolumab              |
| Investigational medicinal product code | BMS-936558             |
| Other name                             |                        |
| Pharmaceutical forms                   | Solution for injection |
| Routes of administration               | Intravenous use        |

Dosage and administration details:

3 mg/kg every 2 weeks for a maximum of 24 months

|                  |                    |
|------------------|--------------------|
| <b>Arm title</b> | Metastatic Combo B |
|------------------|--------------------|

Arm description:

Nivolumab 1 mg/kg IV over 30 minutes + Ipilimumab 3 mg/kg IV over 30 minutes every 3 weeks for 4

doses followed by Nivolumab 240 mg IV over 30 minutes every 2 weeks for a maximum of 24 months or until disease progression, unacceptable toxicity, or withdrawal of consent, whichever comes first

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

Dosage and administration details:

3 mg/kg every 3 weeks for 4 doses

|  |                        |
|--|------------------------|
| Investigational medicinal product name | Nivolumab              |
| Investigational medicinal product code | BMS-936558             |
| Other name                             |                        |
| Pharmaceutical forms                   | Solution for injection |
| Routes of administration               | Intravenous use        |

Dosage and administration details:

1 mg/kg every 3 weeks for 4 doses followed by 240 mg every 2 weeks for a maximum of 24 months

|                  |                    |
|------------------|--------------------|
| <b>Arm title</b> | Metastatic Combo C |
|------------------|--------------------|

Arm description:

Nivolumab 240 mg IV over 30 minutes + BMS-986016 (Relatlimab) 80 mg IV over 60 minutes administered every 2 weeks for a maximum of 24 months, or until disease progression, unacceptable toxicity, or withdrawal of consent, whichever comes first

|  |                 |
|--|-----------------|
| Arm type                               | Experimental    |
| Investigational medicinal product name | Relatlimab      |
| Investigational medicinal product code | BMS-986016      |
| Other name                             |                 |
| Pharmaceutical forms                   | Injection       |
| Routes of administration               | Intravenous use |

Dosage and administration details:

80 mg every 2 weeks for a maximum of 24 months

|  |                        |
|--|------------------------|
| Investigational medicinal product name | Nivolumab              |
| Investigational medicinal product code | BMS-936558             |
| Other name                             |                        |
| Pharmaceutical forms                   | Solution for injection |
| Routes of administration               | Intravenous use        |

Dosage and administration details:

240 mg every 2 weeks for a maximum of 24 months

|                  |                    |
|------------------|--------------------|
| <b>Arm title</b> | Metastatic Combo D |
|------------------|--------------------|

Arm description:

Daratumumab 16 mg/kg IV weekly for the first 8 weeks. Starting at Week 3, Nivolumab 240 mg IV over 30 minutes every 2 weeks. Daratumumab 16 mg/kg every 2 weeks from Weeks 9-24. Starting at Week 25, Nivolumab 480 mg IV flat dose over 30 minutes every 4 weeks; daratumumab 16 mg/kg every 4 weeks for a maximum of 24 months or until progression, unacceptable toxicity, or withdrawal of consent, whichever comes first

|  |                 |
|--|-----------------|
| Arm type                               | Experimental    |
| Investigational medicinal product name | Daratumumab     |
| Investigational medicinal product code |                 |
| Other name                             |                 |
| Pharmaceutical forms                   | Injection       |
| Routes of administration               | Intravenous use |

Dosage and administration details:

16 mg/kg weekly for the first 8 weeks and then every 2 weeks from weeks 9-24

|  |                        |
|--|------------------------|
| Investigational medicinal product name | Nivolumab              |
| Investigational medicinal product code | BMS-936558             |
| Other name                             |                        |
| Pharmaceutical forms                   | Solution for injection |
| Routes of administration               | Intravenous use        |

Dosage and administration details:

Starting at week 3, 240 mg every 2 weeks and then starting at week 25, 480 mg every 4 weeks for a maximum of 24 months

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

Arm description:

Nivolumab administered intravenously (IV) over 30 minutes at 240 mg for 2 doses, on Day 1 and Day 15

|  |                        |
|--|------------------------|
| Arm type                               | Experimental           |
| Investigational medicinal product name | Nivolumab              |
| Investigational medicinal product code | BMS-936558             |
| Other name                             |                        |
| Pharmaceutical forms                   | Solution for injection |
| Routes of administration               | Intravenous use        |

Dosage and administration details:

240 mg for 2 doses, on Day 1 and Day 15

| Number of subjects in period 1                     | Metastatic Monotherapy | Metastatic Combo A | Metastatic Combo B |
|--|------------------------|--------------------|--------------------|
| Started  | 113                    | 195                | 133                |
| Completed  | 0                      | 0                  | 0                  |
| Not completed                                      | 113                    | 195                | 133                |
| Consent withdrawn by subject                       | 4                      | -                  | 3                  |
| Disease progression                                | 73                     | 111                | 62                 |
| Study drug toxicity                                | 11                     | 33                 | 31                 |
| Maximum clinical benefit                           | 3                      | -                  | 1                  |
| Adverse event unrelated to study drug              | 9                      | 11                 | 7                  |
| Other reasons                                      | 7                      | 32                 | 23                 |
| Lost to follow-up                                  | -                      | -                  | 2                  |
| Participant request to discontinue study treatment | 6                      | 8                  | 4                  |

| Number of subjects in period 1 | Metastatic Combo C | Metastatic Combo D | Neoadjuvant |
|--------------------------------|--------------------|--------------------|-------------|
| Started                        | 8                  | 6                  | 123         |
| Completed                      | 0                  | 0                  | 116         |
| Not completed                  | 8                  | 6                  | 7           |
| Consent withdrawn by subject   | -                  | -                  | 2           |
| Disease progression            | 7                  | 4                  | 2           |
| Study drug toxicity            | -                  | -                  | 2           |
| Maximum clinical benefit       | -                  | -                  | -           |

|  |   |   |   |
|--|---|---|---|
| Adverse event unrelated to study drug              | - | 1 | - |
| Other reasons                                      | 1 | 1 | 1 |
| Lost to follow-up                                  | - | - | - |
| Participant request to discontinue study treatment | - | - | - |

## Baseline characteristics

### Reporting groups

|   |                        |
|---|------------------------|
| Reporting group title   | Metastatic Monotherapy |
| Reporting group description:<br>Nivolumab IV over 30 minutes at 240 mg every 2 weeks for a maximum of 24 months or until disease progression, unacceptable toxicity, or withdrawal of consent, whichever comes first  |                        |
| Reporting group title   | Metastatic Combo A     |
| Reporting group description:<br>Nivolumab 3 mg/kg IV over 30 minutes every 2 weeks + Ipilimumab 1 mg/kg IV over 30 minutes every 6 weeks for a maximum of 24 months or until disease progression, unacceptable toxicity, or withdrawal of consent, whichever comes first  |                        |
| Reporting group title   | Metastatic Combo B     |
| Reporting group description:<br>Nivolumab 1 mg/kg IV over 30 minutes + Ipilimumab 3 mg/kg IV over 30 minutes every 3 weeks for 4 doses followed by Nivolumab 240 mg IV over 30 minutes every 2 weeks for a maximum of 24 months or until disease progression, unacceptable toxicity, or withdrawal of consent, whichever comes first  |                        |
| Reporting group title   | Metastatic Combo C     |
| Reporting group description:<br>Nivolumab 240 mg IV over 30 minutes + BMS-986016 (Relatlimab) 80 mg IV over 60 minutes administered every 2 weeks for a maximum of 24 months, or until disease progression, unacceptable toxicity, or withdrawal of consent, whichever comes first  |                        |
| Reporting group title   | Metastatic Combo D     |
| Reporting group description:<br>Daratumumab 16 mg/kg IV weekly for the first 8 weeks. Starting at Week 3, Nivolumab 240 mg IV over 30 minutes every 2 weeks. Daratumumab 16 mg/kg every 2 weeks from Weeks 9-24. Starting at Week 25, Nivolumab 480 mg IV flat dose over 30 minutes every 4 weeks; daratumumab 16 mg/kg every 4 weeks for a maximum of 24 months or until progression, unacceptable toxicity, or withdrawal of consent, whichever comes first |                        |
| Reporting group title   | Neoadjuvant            |
| Reporting group description:<br>Nivolumab administered intravenously (IV) over 30 minutes at 240 mg for 2 doses, on Day 1 and Day 15  |                        |

| Reporting group values    | Metastatic Monotherapy | Metastatic Combo A | Metastatic Combo B |
|---------------------------|------------------------|--------------------|--------------------|
| Number of subjects        | 113                    | 195                | 133                |
| Age categorical<br>Units: |                        |                    |                    |

|  |        |        |        |
|--|--------|--------|--------|
| Age Continuous<br>Units: years           |        |        |        |
| arithmetic mean                          | 57.4   | 57.5   | 48.2   |
| standard deviation                       | ± 13.5 | ± 13.2 | ± 12.3 |
| Sex: Female, Male<br>Units: Participants |        |        |        |
| Female                                   | 39     | 85     | 129    |
| Male                                     | 74     | 110    | 4      |
| Race (NIH/OMB)<br>Units: Subjects        |        |        |        |
| American Indian or Alaska Native         | 2      | 0      | 2      |
| Asian                                    | 14     | 31     | 10     |



|   |    |     |     |
|---|----|-----|-----|
| Native Hawaiian or Other Pacific Islander | 0  | 0   | 0   |
| Black or African American                 | 3  | 6   | 5   |
| White                                     | 86 | 147 | 115 |
| More than one race                        | 0  | 0   | 0   |
| Unknown or Not Reported                   | 8  | 11  | 1   |

| Reporting group values    | Metastatic Combo C | Metastatic Combo D | Neoadjuvant |
|---------------------------|--------------------|--------------------|-------------|
| Number of subjects        | 8                  | 6                  | 123         |
| Age categorical<br>Units: |                    |                    |             |

|   |               |                |                |
|---|---------------|----------------|----------------|
| Age Continuous<br>Units: years<br>arithmetic mean<br>standard deviation | 59.0<br>± 7.6 | 66.5<br>± 15.3 | 62.0<br>± 12.7 |
| Sex: Female, Male<br>Units: Participants                                |               |                |                |
| Female  | 1             | 3              | 59             |
| Male  | 7             | 3              | 64             |
| Race (NIH/OMB)<br>Units: Subjects                                       |               |                |                |
| American Indian or Alaska Native  | 0             | 0              | 2              |
| Asian   | 0             | 0              | 1              |
| Native Hawaiian or Other Pacific Islander                               | 0             | 0              | 0              |
| Black or African American   | 0             | 0              | 3              |
| White   | 8             | 6              | 113            |
| More than one race  | 0             | 0              | 0              |
| Unknown or Not Reported   | 0             | 0              | 4              |

| Reporting group values    | Total |  |  |
|---------------------------|-------|--|--|
| Number of subjects        | 578   |  |  |
| Age categorical<br>Units: |       |  |  |

|   |     |  |  |
|---|-----|--|--|
| Age Continuous<br>Units: years<br>arithmetic mean<br>standard deviation | -   |  |  |
| Sex: Female, Male<br>Units: Participants                                |     |  |  |
| Female  | 316 |  |  |
| Male  | 262 |  |  |
| Race (NIH/OMB)<br>Units: Subjects                                       |     |  |  |
| American Indian or Alaska Native  | 6   |  |  |
| Asian   | 56  |  |  |
| Native Hawaiian or Other Pacific Islander                               | 0   |  |  |
| Black or African American   | 17  |  |  |
| White   | 475 |  |  |

|                         |    |  |  |
|-------------------------|----|--|--|
| More than one race      | 0  |  |  |
| Unknown or Not Reported | 24 |  |  |

## End points

### End points reporting groups

|   |                        |
|---|------------------------|
| Reporting group title   | Metastatic Monotherapy |
| Reporting group description:<br>Nivolumab IV over 30 minutes at 240 mg every 2 weeks for a maximum of 24 months or until disease progression, unacceptable toxicity, or withdrawal of consent, whichever comes first  |                        |
| Reporting group title   | Metastatic Combo A     |
| Reporting group description:<br>Nivolumab 3 mg/kg IV over 30 minutes every 2 weeks + Ipilimumab 1 mg/kg IV over 30 minutes every 6 weeks for a maximum of 24 months or until disease progression, unacceptable toxicity, or withdrawal of consent, whichever comes first  |                        |
| Reporting group title   | Metastatic Combo B     |
| Reporting group description:<br>Nivolumab 1 mg/kg IV over 30 minutes + Ipilimumab 3 mg/kg IV over 30 minutes every 3 weeks for 4 doses followed by Nivolumab 240 mg IV over 30 minutes every 2 weeks for a maximum of 24 months or until disease progression, unacceptable toxicity, or withdrawal of consent, whichever comes first  |                        |
| Reporting group title   | Metastatic Combo C     |
| Reporting group description:<br>Nivolumab 240 mg IV over 30 minutes + BMS-986016 (Relatlimab) 80 mg IV over 60 minutes administered every 2 weeks for a maximum of 24 months, or until disease progression, unacceptable toxicity, or withdrawal of consent, whichever comes first  |                        |
| Reporting group title   | Metastatic Combo D     |
| Reporting group description:<br>Daratumumab 16 mg/kg IV weekly for the first 8 weeks. Starting at Week 3, Nivolumab 240 mg IV over 30 minutes every 2 weeks. Daratumumab 16 mg/kg every 2 weeks from Weeks 9-24. Starting at Week 25, Nivolumab 480 mg IV flat dose over 30 minutes every 4 weeks; daratumumab 16 mg/kg every 4 weeks for a maximum of 24 months or until progression, unacceptable toxicity, or withdrawal of consent, whichever comes first |                        |
| Reporting group title   | Neoadjuvant            |
| Reporting group description:<br>Nivolumab administered intravenously (IV) over 30 minutes at 240 mg for 2 doses, on Day 1 and Day 15  |                        |

### Primary: Neoadjuvant: Number of Participants with Drug-Related Select Adverse Events (AEs)

|  |   |
|--|---|
| End point title  | Neoadjuvant: Number of Participants with Drug-Related Select Adverse Events (AEs) <sup>[1][2]</sup> |
| End point description:<br>Number of participants with any grade of drug-related select adverse events (AEs) including endocrine, gastrointestinal, hepatic, pulmonary, renal, skin, and hypersensitivity AEs in Neoadjuvant cohort   |   |
| End point type   | Primary   |
| End point timeframe:<br>From first dose to 30 days post last dose (Up to 2 months)   |   |
| Notes:<br>[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.<br>Justification: only summary analysis planned for this endpoint<br>[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.<br>Justification: Only specified arms planned for this endpoint |   |

| End point values                       | Neoadjuvant     |  |  |  |
|--|-----------------|--|--|--|
| Subject group type                     | Reporting group |  |  |  |
| Number of subjects analysed            | 123             |  |  |  |
| Units: Participants                    |                 |  |  |  |
| Endocrine AEs                          | 3               |  |  |  |
| Gastrointestinal AEs                   | 4               |  |  |  |
| Hepatic AEs                            | 3               |  |  |  |
| Pulmonary AEs                          | 0               |  |  |  |
| Renal AEs                              | 0               |  |  |  |
| Skin AEs                               | 9               |  |  |  |
| Hypersensitivity/Infusion Reaction AEs | 5               |  |  |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: Neoadjuvant: Rate of Surgery Delay

|   |  |
|---|--|
| End point title   | Neoadjuvant: Rate of Surgery Delay <sup>[3]</sup> <sup>[4]</sup> |
| End point description:  |  |
| Rate of surgery delay is defined as the percentage of participants in the neoadjuvant cohort with surgery delayed > 4 weeks from the planned surgery date or planned start date for chemoradiation due to a drug-related adverse event. |  |
| Participants with the following diseases will be assessed:  |  |
| 1. HPV positive squamous cell carcinoma of the Head and Neck (SCCHN);   |  |
| 2. HPV negative SCCHN;  |  |
| 3. Cervical Carcinoma;  |  |
| 4. Vaginal/Vulvar Carcinoma;  |  |
| 5. Merkel Cell Carcinoma  |  |
| End point type  | Primary  |
| End point timeframe:  |  |
| Day 29  |  |

Notes:

[3] - 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: only summary analysis planned for this endpoint

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Only specified arms planned for this endpoint

| End point values                  | Neoadjuvant       |  |  |  |
|-----------------------------------|-------------------|--|--|--|
| Subject group type                | Reporting group   |  |  |  |
| Number of subjects analysed       | 112               |  |  |  |
| Units: Percentage of participants |                   |  |  |  |
| number (confidence interval 95%)  |                   |  |  |  |
| HPV positive SCCHN                | 0 (0 to 13.7)     |  |  |  |
| HPV negative SCCHN                | 0 (0 to 13.7)     |  |  |  |
| Cervical Carcinoma                | 7.7 (0.2 to 36.0) |  |  |  |
| Vaginal/Vulvar Carcinoma          | 0 (0.0 to 26.5)   |  |  |  |
| Merkel Cell Carcinoma             | 2.7 (0.1 to 14.2) |  |  |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: Neoadjuvant: Number of Participants with Drug-Related Serious Adverse Events (SAEs)

|                 |   |
|-----------------|---|
| End point title | Neoadjuvant: Number of Participants with Drug-Related Serious Adverse Events (SAEs) <sup>[5][6]</sup> |
|-----------------|---|

End point description:

Number of participants with any grade of drug-related serious adverse events (SAEs) in Neoadjuvant cohort

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

End point timeframe:

From first dose to 30 days post last dose (Up to 2 months)

Notes:

[5] - 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: only summary analysis planned for this endpoint

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Only specified arms planned for this endpoint

|                             |                 |  |  |  |
|-----------------------------|-----------------|--|--|--|
| End point values            | Neoadjuvant     |  |  |  |
| Subject group type          | Reporting group |  |  |  |
| Number of subjects analysed | 123             |  |  |  |
| Units: Participants         | 6               |  |  |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: Metastatic: Investigator-Assessed Objective Response Rate (ORR)

|                 |   |
|-----------------|---|
| End point title | Metastatic: Investigator-Assessed Objective Response Rate (ORR) <sup>[7][8]</sup> |
|-----------------|---|

End point description:

Objective response rate (ORR) is defined as the percentage of participants with a best overall response (BOR) of confirmed complete response (CR) or partial response (PR) using RECIST 1.1 criteria. An ORR in excess of 10% will be considered of clinical interest, and an ORR of 25% or greater will be considered of strong clinical interest.

Complete Response (CR): Disappearance of all target lesions. Any pathological lymph nodes (whether target or non-target) must have reduction in short axis to < 10 mm.

Partial Response (PR): At least a 30% decrease in the sum of diameters of target lesions, taking as reference the baseline sum diameters.

Participants with the following diseases will be assessed:

1. EBV positive related gastric cancer;
2. HPV positive SCCHN;
3. Other anogenital HPV associated cancers;

4. GYN (Cervical, Vaginal, Vulvar) carcinoma;  
5. Merkel cell carcinoma (MCC);  
6. Nasopharyngeal carcinoma (NPC)  
99999=NA

|  |         |
|--|---------|
| End point type   | Primary |
| End point timeframe:   |         |
| From the date of first dose to the date of the initial objectively documented tumor progression or the date of the last tumor assessment prior to subsequent therapy (Up to 72 months) |         |

Notes:

[7] - 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: only summary analysis planned for this endpoint

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Only specified arms planned for this endpoint

| End point values                        | Metastatic Monotherapy | Metastatic Combo A     | Metastatic Combo B     | Metastatic Combo C     |
|---|------------------------|------------------------|------------------------|------------------------|
| Subject group type                      | Reporting group        | Reporting group        | Reporting group        | Reporting group        |
| Number of subjects analysed             | 113                    | 195                    | 133                    | 8                      |
| Units: Percentage of participants       |                        |                        |                        |                        |
| number (confidence interval 95%)        |                        |                        |                        |                        |
| EBV positive related gastric cancer     | 14.3 (1.8 to 42.8)     | 99999 (99999 to 99999) | 99999 (99999 to 99999) | 99999 (99999 to 99999) |
| HPV positive SCCHN                      | 11.5 (2.4 to 30.2)     | 31.0 (17.6 to 47.1)    | 99999 (99999 to 99999) | 0 (0.0 to 36.9)        |
| Other anogenital HPV associated cancers | 99999 (99999 to 99999) | 34.8 (16.4 to 57.3)    | 28.6 (11.3 to 52.2)    | 99999 (99999 to 99999) |
| SCCHN I-O naive                         | 99999 (99999 to 99999) | 99999 (99999 to 99999) | 99999 (99999 to 99999) | 99999 (99999 to 99999) |
| Cervical                                | 26.3 (9.1 to 51.2)     | 31.1 (18.2 to 46.6)    | 40.0 (25.7 to 55.7)    | 99999 (99999 to 99999) |
| Cervical first line                     | 99999 (99999 to 99999) | 99999 (99999 to 99999) | 36.4 (22.4 to 52.2)    | 99999 (99999 to 99999) |
| Cervical second line                    | 99999 (99999 to 99999) | 99999 (99999 to 99999) | 39.1 (19.7 to 61.5)    | 99999 (99999 to 99999) |
| Vaginal/Vulvar                          | 20.0 (0.5 to 71.6)     | 99999 (99999 to 99999) | 99999 (99999 to 99999) | 99999 (99999 to 99999) |
| MCC                                     | 64.0 (42.5 to 82.0)    | 58.1 (42.1 to 73.0)    | 99999 (99999 to 99999) | 99999 (99999 to 99999) |
| NPC                                     | 16.7 (4.7 to 37.4)     | 26.2 (13.9 to 42.0)    | 99999 (99999 to 99999) | 99999 (99999 to 99999) |

| End point values                        | Metastatic Combo D     |  |  |  |
|---|------------------------|--|--|--|
| Subject group type                      | Reporting group        |  |  |  |
| Number of subjects analysed             | 6                      |  |  |  |
| Units: Percentage of participants       |                        |  |  |  |
| number (confidence interval 95%)        |                        |  |  |  |
| EBV positive related gastric cancer     | 99999 (99999 to 99999) |  |  |  |
| HPV positive SCCHN                      | 99999 (99999 to 99999) |  |  |  |
| Other anogenital HPV associated cancers | 99999 (99999 to 99999) |  |  |  |

|                      |                        |  |  |  |
|----------------------|------------------------|--|--|--|
| SCCHN I-O naive      | 16.7 (0.4 to 64.1)     |  |  |  |
| Cervical             | 99999 (99999 to 99999) |  |  |  |
| Cervical first line  | 99999 (99999 to 99999) |  |  |  |
| Cervical second line | 99999 (99999 to 99999) |  |  |  |
| Vaginal/Vulvar       | 99999 (99999 to 99999) |  |  |  |
| MCC                  | 99999 (99999 to 99999) |  |  |  |
| NPC                  | 99999 (99999 to 99999) |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Metastatic: Investigator-Assessed Duration of Response (DoR)

|                 |  |
|-----------------|--|
| End point title | Metastatic: Investigator-Assessed Duration of Response |
|-----------------|--|

End point description:

Duration of response (DoR) is defined as the time from first confirmed response (complete response or partial response) to the date of the initial objectively documented tumor progression as determined per investigator assessment using RECIST 1.1 criteria or death due to any cause, whichever occurs first. Participants with the following diseases will be assessed:

1. EBV positive related gastric cancer;
2. HPV positive SCCHN;
3. Other anogenital HPV associated cancers;
4. GYN (Cervical, Vaginal, Vulvar) carcinoma;
5. Merkel cell carcinoma (MCC);
6. Nasopharyngeal carcinoma (NPC)

NOTE: "Cervical, Randomized" and "Cervical, Pooled" are not mutually exclusive categories.  
99999=NA

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

End point timeframe:

From first confirmed response (complete response or partial response) to the date of the initial objectively documented tumor progression or death due to any cause, whichever occurs first (Up to 83 months)

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.  
Justification: Only specified arms planned for this endpoint

| End point values                        | Metastatic Monotherapy | Metastatic Combo A     | Metastatic Combo B     | Metastatic Combo C |
|---|------------------------|------------------------|------------------------|--------------------|
| Subject group type                      | Reporting group        | Reporting group        | Reporting group        | Reporting group    |
| Number of subjects analysed             | 30 <sup>[10]</sup>     | 72 <sup>[11]</sup>     | 50 <sup>[12]</sup>     | 0 <sup>[13]</sup>  |
| Units: Months                           |                        |                        |                        |                    |
| median (confidence interval 95%)        |                        |                        |                        |                    |
| EBV positive related gastric cancer     | 99999 (99999 to 99999) | 99999 (99999 to 99999) | 99999 (99999 to 99999) | ( to )             |
| HPV positive SCCHN                      | 44.25 (24.90 to 99999) | 34.46 (10.45 to 99999) | 99999 (99999 to 99999) | ( to )             |
| Other anogenital HPV associated cancers | 99999 (99999 to 99999) | 18.23 (3.68 to 27.93)  | 3.71 (3.58 to 99999)   | ( to )             |

|                      |                        |                        |                        |        |
|----------------------|------------------------|------------------------|------------------------|--------|
| SCCHN I-O naive      | 99999 (99999 to 99999) | 99999 (99999 to 99999) | 99999 (99999 to 99999) | ( to ) |
| Cervical, Randomized | 99999 (35.29 to 99999) | 99999 (8.67 to 99999)  | 34.07 (15.28 to 99999) | ( to ) |
| Cervical, Pooled     | 99999 (99999 to 99999) | 99999 (99999 to 99999) | 34.07 (15.28 to 99999) | ( to ) |
| Vaginal/Vulvar       | 4.96 (-99999 to 99999) | 99999 (99999 to 99999) | 99999 (99999 to 99999) | ( to ) |
| MCC                  | 60.62 (16.72 to 99999) | 25.86 (10.38 to 99999) | 99999 (99999 to 99999) | ( to ) |
| NPC                  | 9.46 (3.68 to 99999)   | 19.63 (5.55 to 99999)  | 99999 (99999 to 99999) | ( to ) |

Notes:

[10] - EBV N=2

HPV N=3

Other HPV N=0

SCCHN N=0

Cervical, R N=5

Cervical, P N=0

Vaginal N=1

MCC N=15

NPC N=4

[11] - EBV N=0

HPV N=13

Other HPV N=8

SCCHN N=0

Cerv. R N=14

Cerv. P N=0

Vaginal N=0

MCC N=25

NPC N=12

[12] - EBV N=0

HPV N=0

Other HPV N=5

SCCHN N=0

Cervical R N=18

Cervical P N=45

Vaginal N=0

MCC N=0

NPC N=0

[13] - 0 complete and partial responders

| End point values                        | Metastatic Combo D     |  |  |  |
|---|------------------------|--|--|--|
| Subject group type                      | Reporting group        |  |  |  |
| Number of subjects analysed             | 1 <sup>[14]</sup>      |  |  |  |
| Units: Months                           |                        |  |  |  |
| median (confidence interval 95%)        |                        |  |  |  |
| EBV positive related gastric cancer     | 99999 (99999 to 99999) |  |  |  |
| HPV positive SCCHN                      | 99999 (99999 to 99999) |  |  |  |
| Other anogenital HPV associated cancers | 99999 (99999 to 99999) |  |  |  |
| SCCHN I-O naive                         | 99999 (99999 to 99999) |  |  |  |
| Cervical, Randomized                    | 99999 (99999 to 99999) |  |  |  |
| Cervical, Pooled                        | 99999 (99999 to 99999) |  |  |  |
| Vaginal/Vulvar                          | 99999 (99999 to 99999) |  |  |  |
| MCC                                     | 99999 (99999 to 99999) |  |  |  |



|     |                        |  |  |  |
|-----|------------------------|--|--|--|
| NPC | 99999 (99999 to 99999) |  |  |  |
|-----|------------------------|--|--|--|

Notes:

[14] - EBV N=0  
 HPV N=0  
 Other HPV N=0  
 SCCHN N=1  
 Cervical, R N=0  
 Cervical, P N=0  
 Vaginal N=0  
 MCC N=0  
 NPC N=0

## Statistical analyses

No statistical analyses for this end point

## Secondary: Metastatic: Overall Survival (OS)

|                 |   |
|-----------------|---|
| End point title | Metastatic: Overall Survival (OS) <sup>[15]</sup> |
|-----------------|---|

End point description:

Overall survival (OS) is defined as the time from first dosing date to the date of death. A participant who has not died will be censored at last known date alive. Participants with the following diseases will be assessed:

1. EBV positive related gastric cancer;
2. HPV positive SCCHN;
3. Other anogenital HPV associated cancers;
4. GYN (Cervical, Vaginal, Vulvar) carcinoma;
5. Merkel cell carcinoma (MCC);
6. Nasopharyngeal carcinoma (NPC)

99999=NA

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

End point timeframe:

From the first dosing date to the date of death (Up to 83 months)

Notes:

[15] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Only specified arms planned for this endpoint

| End point values                        | Metastatic Monotherapy | Metastatic Combo A     | Metastatic Combo B     | Metastatic Combo C     |
|---|------------------------|------------------------|------------------------|------------------------|
| Subject group type                      | Reporting group        | Reporting group        | Reporting group        | Reporting group        |
| Number of subjects analysed             | 113                    | 195                    | 133                    | 8                      |
| Units: Months                           |                        |                        |                        |                        |
| median (confidence interval 95%)        |                        |                        |                        |                        |
| EBV positive related gastric cancer     | 9.99 (3.09 to 30.13)   | 99999 (99999 to 99999) | 99999 (99999 to 99999) | 99999 (99999 to 99999) |
| HPV positive SCCHN                      | 20.44 (13.90 to 36.50) | 17.08 (9.49 to 26.78)  | 99999 (99999 to 99999) | 8.84 (2.50 to 35.06)   |
| Other anogenital HPV associated cancers | 99999 (99999 to 99999) | 12.12 (6.83 to 29.54)  | 14.06 (4.37 to 30.59)  | 99999 (99999 to 99999) |
| SCCHN I-O naive                         | 99999 (99999 to 99999) | 99999 (99999 to 99999) | 99999 (99999 to 99999) | 99999 (99999 to 99999) |
| Cervical, Randomized                    | 21.55 (8.25 to 44.85)  | 17.12 (10.22 to 34.79) | 22.74 (14.62 to 32.82) | 99999 (99999 to 99999) |
| Vaginal/Vulvar                          | 10.28 (3.88 to 23.72)  | 99999 (99999 to 99999) | 99999 (99999 to 99999) | 99999 (99999 to 99999) |
| MCC                                     | 80.66 (23.26 to 99999) | 29.83 (8.51 to 48.33)  | 99999 (99999 to 99999) | 99999 (99999 to 99999) |
| NPC                                     | 22.74 (12.62 to 35.29) | 23.66 (16.82 to 41.43) | 99999 (99999 to 99999) | 99999 (99999 to 99999) |

| End point values                        | Metastatic Combo D     |  |  |  |
|---|------------------------|--|--|--|
| Subject group type                      | Reporting group        |  |  |  |
| Number of subjects analysed             | 6                      |  |  |  |
| Units: Months                           |                        |  |  |  |
| median (confidence interval 95%)        |                        |  |  |  |
| EBV positive related gastric cancer     | 99999 (99999 to 99999) |  |  |  |
| HPV positive SCCHN                      | 99999 (99999 to 99999) |  |  |  |
| Other anogenital HPV associated cancers | 99999 (99999 to 99999) |  |  |  |
| SCCHN I-O naive                         | 4.21 (1.68 to 99999)   |  |  |  |
| Cervical, Randomized                    | 99999 (99999 to 99999) |  |  |  |
| Vaginal/Vulvar                          | 99999 (99999 to 99999) |  |  |  |
| MCC                                     | 99999 (99999 to 99999) |  |  |  |
| NPC                                     | 99999 (99999 to 99999) |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Metastatic: Investigator-Assessed Progression-Free Survival (PFS)

|                 |   |
|-----------------|---|
| End point title | Metastatic: Investigator-Assessed Progression-Free Survival (PFS) <sup>[16]</sup> |
|-----------------|---|

End point description:

Investigator-assessed progression free survival (PFS) is defined as the time from first dosing date to the date of the first documented tumor progression, as determined by investigators (per RECIST 1.1), or death due to any cause, whichever occurs first. Participants with the following diseases will be assessed:

1. EBV positive related gastric cancer;
2. HPV positive SCCHN;
3. Other anogenital HPV associated cancers;
4. GYN (Cervical, Vaginal, Vulvar) carcinoma;
5. Merkel cell carcinoma (MCC);
6. Nasopharyngeal carcinoma (NPC)

99999=NA

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

End point timeframe:

From the first dosing date to the date of the first documented tumor progression or death due to any cause, whichever occurs first (Up to 83 months)

Notes:

[16] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Only specified arms planned for this endpoint

| End point values                        | Metastatic Monotherapy | Metastatic Combo A     | Metastatic Combo B     | Metastatic Combo C     |
|---|------------------------|------------------------|------------------------|------------------------|
| Subject group type                      | Reporting group        | Reporting group        | Reporting group        | Reporting group        |
| Number of subjects analysed             | 113                    | 195                    | 133                    | 8                      |
| Units: Months                           |                        |                        |                        |                        |
| median (confidence interval 95%)        |                        |                        |                        |                        |
| EBV positive related gastric cancer     | 2.94 (1.05 to 3.75)    | 99999 (99999 to 99999) | 99999 (99999 to 99999) | 99999 (99999 to 99999) |
| HPV positive SCCHN                      | 3.25 (1.84 to 6.93)    | 3.71 (1.77 to 6.80)    | 99999 (99999 to 99999) | 3.81 (1.77 to 7.39)    |
| Other anogenital HPV associated cancers | 99999 (99999 to 99999) | 4.63 (1.94 to 14.29)   | 3.58 (2.04 to 7.49)    | 99999 (99999 to 99999) |
| SCCHN I-O naive                         | 99999 (99999 to 99999) | 99999 (99999 to 99999) | 99999 (99999 to 99999) | 99999 (99999 to 99999) |
| Cervical, Randomized                    | 5.09 (1.87 to 9.07)    | 3.75 (3.32 to 9.23)    | 7.11 (3.71 to 17.25)   | 99999 (99999 to 99999) |
| Vaginal/Vulvar                          | 3.75 (1.22 to 8.15)    | 99999 (99999 to 99999) | 99999 (99999 to 99999) | 99999 (99999 to 99999) |
| MCC                                     | 21.32 (9.20 to 62.52)  | 8.39 (3.71 to 24.34)   | 99999 (99999 to 99999) | 99999 (99999 to 99999) |
| NPC                                     | 1.94 (1.54 to 3.58)    | 5.36 (2.37 to 9.23)    | 99999 (99999 to 99999) | 99999 (99999 to 99999) |

| End point values                        | Metastatic Combo D     |  |  |  |
|---|------------------------|--|--|--|
| Subject group type                      | Reporting group        |  |  |  |
| Number of subjects analysed             | 6                      |  |  |  |
| Units: Months                           |                        |  |  |  |
| median (confidence interval 95%)        |                        |  |  |  |
| EBV positive related gastric cancer     | 99999 (99999 to 99999) |  |  |  |
| HPV positive SCCHN                      | 99999 (99999 to 99999) |  |  |  |
| Other anogenital HPV associated cancers | 99999 (99999 to 99999) |  |  |  |
| SCCHN I-O naive                         | 1.81 (1.08 to 99999)   |  |  |  |
| Cervical, Randomized                    | 99999 (99999 to 99999) |  |  |  |
| Vaginal/Vulvar                          | 99999 (99999 to 99999) |  |  |  |
| MCC                                     | 99999 (99999 to 99999) |  |  |  |
| NPC                                     | 99999 (99999 to 99999) |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Post-hoc: Metastatic: Investigator-Assessed Objective Response Rate (ORR) Extended Collection

|                 |   |
|-----------------|---|
| End point title | Metastatic: Investigator-Assessed Objective Response Rate |
|-----------------|---|

## End point description:

ORR is defined as the percentage of participants with a best overall response (BOR) of confirmed complete response (CR) or partial response (PR) using RECIST 1.1 criteria. An ORR in excess of 10% will be considered of clinical interest, and an ORR of 25% or greater will be considered of strong clinical interest.

Complete Response (CR): Disappearance of all target lesions. Any pathological lymph nodes (whether target or non-target) must have reduction in short axis to < 10 mm.

Partial Response (PR): At least a 30% decrease in the sum of diameters of target lesions, taking as reference the baseline sum diameters.

Participants with the following diseases will be assessed:

1. EBV positive related gastric cancer;
2. HPV positive SCCHN;
3. Other anogenital HPV associated cancers;
4. GYN (Cervical, Vaginal, Vulvar) carcinoma;
5. Merkel cell carcinoma (MCC);
6. Nasopharyngeal carcinoma (NPC)

Note: "Cervical, Randomized" and "Cervical, Pooled" are not mutually exclusive categories

99999=NA

|                |          |
|----------------|----------|
| End point type | Post-hoc |
|----------------|----------|

## End point timeframe:

From the date of first dose to the date of the initial objectively documented tumor progression or the date of the last tumor assessment prior to subsequent therapy (Up to 83 months)

## Notes:

[17] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Only specified arms planned for this endpoint

| End point values                        | Metastatic Monotherapy | Metastatic Combo A     | Metastatic Combo B     | Metastatic Combo C     |
|---|------------------------|------------------------|------------------------|------------------------|
| Subject group type                      | Reporting group        | Reporting group        | Reporting group        | Reporting group        |
| Number of subjects analysed             | 113                    | 195                    | 133                    | 8                      |
| Units: Percentage of participants       |                        |                        |                        |                        |
| number (confidence interval 95%)        |                        |                        |                        |                        |
| EBV positive related gastric cancer     | 14.3 (1.8 to 42.8)     | 99999 (99999 to 99999) | 99999 (99999 to 99999) | 99999 (99999 to 99999) |
| HPV positive SCCHN                      | 11.5 (2.4 to 30.2)     | 31.0 (17.6 to 47.1)    | 99999 (99999 to 99999) | 0 (0.0 to 36.9)        |
| Other anogenital HPV associated cancers | 99999 (99999 to 99999) | 34.8 (16.4 to 57.3)    | 23.8 (8.2 to 47.2)     | 99999 (99999 to 99999) |
| SCCHN I-O naive                         | 99999 (99999 to 99999) | 99999 (99999 to 99999) | 99999 (99999 to 99999) | 99999 (99999 to 99999) |
| Cervical, Randomized                    | 26.3 (9.1 to 51.2)     | 31.1 (18.2 to 46.6)    | 99999 (99999 to 99999) | 99999 (99999 to 99999) |
| Cervical, Pooled                        | 99999 (99999 to 99999) | 99999 (99999 to 99999) | 40.2 (31.0 to 49.9)    | 99999 (99999 to 99999) |
| Vaginal/Vulvar                          | 20.0 (0.5 to 71.6)     | 99999 (99999 to 99999) | 99999 (99999 to 99999) | 99999 (99999 to 99999) |
| MCC                                     | 60.0 (38.7 to 78.9)    | 58.1 (42.1 to 73.0)    | 99999 (99999 to 99999) | 99999 (99999 to 99999) |
| NPC                                     | 16.7 (4.7 to 37.4)     | 28.6 (15.7 to 44.6)    | 99999 (99999 to 99999) | 99999 (99999 to 99999) |

| End point values            | Metastatic Combo D |  |  |  |
|-----------------------------|--------------------|--|--|--|
| Subject group type          | Reporting group    |  |  |  |
| Number of subjects analysed | 6                  |  |  |  |

|   |                        |  |  |  |
|---|------------------------|--|--|--|
| Units: Percentage of participants       |                        |  |  |  |
| number (confidence interval 95%)        |                        |  |  |  |
| EBV positive related gastric cancer     | 99999 (99999 to 99999) |  |  |  |
| HPV positive SCCHN                      | 99999 (99999 to 99999) |  |  |  |
| Other anogenital HPV associated cancers | 99999 (99999 to 99999) |  |  |  |
| SCCHN I-O naive                         | 16.7 (0.4 to 64.1)     |  |  |  |
| Cervical, Randomized                    | 99999 (99999 to 99999) |  |  |  |
| Cervical, Pooled                        | 99999 (99999 to 99999) |  |  |  |
| Vaginal/Vulvar                          | 99999 (99999 to 99999) |  |  |  |
| MCC                                     | 99999 (99999 to 99999) |  |  |  |
| NPC                                     | 99999 (99999 to 99999) |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

SAEs and NSAEs are assessed from first dose to 100 days post last dose (Up to 83 months) Participants were assessed for deaths (all-causes) from their first dose to their study completion (Up to 84 months)

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

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 25.1 |
|--------------------|------|

### Reporting groups

|                       |                        |
|-----------------------|------------------------|
| Reporting group title | Metastatic Monotherapy |
|-----------------------|------------------------|

Reporting group description:

Nivolumab IV over 30 minutes at 240 mg every 2 weeks for a maximum of 24 months or until disease progression, unacceptable toxicity, or withdrawal of consent, whichever comes first

|                       |             |
|-----------------------|-------------|
| Reporting group title | Neoadjuvant |
|-----------------------|-------------|

Reporting group description:

Nivolumab IV over 30 minutes at 240 mg for 2 doses, on Day 1 and Day 15

|                       |                    |
|-----------------------|--------------------|
| Reporting group title | Metastatic Combo D |
|-----------------------|--------------------|

Reporting group description:

Daratumumab 16 mg/kg IV weekly for the first 8 weeks. Starting at Week 3, Nivolumab 240 mg IV over 30 minutes every 2 weeks. Daratumumab 16 mg/kg every 2 weeks from Weeks 9-24. Starting at Week 25, Nivolumab 480 mg IV flat dose over 30 minutes every 4 weeks; daratumumab 16 mg/kg every 4 weeks for a maximum of 24 months or until progression, unacceptable toxicity, or withdrawal of consent, whichever comes first

|                       |                    |
|-----------------------|--------------------|
| Reporting group title | Metastatic Combo B |
|-----------------------|--------------------|

Reporting group description:

Nivolumab 1 mg/kg IV over 30 minutes + Ipilimumab 3 mg/kg IV over 30 minutes every 3 weeks for 4 doses followed by Nivolumab 240 mg IV over 30 minutes every 2 weeks for a maximum of 24 months or until disease progression, unacceptable toxicity, or withdrawal of consent, whichever comes first

|                       |                    |
|-----------------------|--------------------|
| Reporting group title | Metastatic Combo C |
|-----------------------|--------------------|

Reporting group description:

Nivolumab 240 mg IV over 30 minutes + BMS-986016 (Relatlimab) 80 mg IV over 60 minutes administered every 2 weeks for a maximum of 24 months, or until disease progression, unacceptable toxicity, or withdrawal of consent, whichever comes first

|                       |                    |
|-----------------------|--------------------|
| Reporting group title | Metastatic Combo A |
|-----------------------|--------------------|

Reporting group description:

Nivolumab 3 mg/kg IV over 30 minutes every 2 weeks + Ipilimumab 1 mg/kg IV over 30 minutes every 6 weeks for a maximum of 24 months or until disease progression, unacceptable toxicity, or withdrawal of consent, whichever comes first

| Serious adverse events  | Metastatic Monotherapy | Neoadjuvant       | Metastatic Combo D |
|---|------------------------|-------------------|--------------------|
| Total subjects affected by serious adverse events                   |                        |                   |                    |
| subjects affected / exposed   | 59 / 113 (52.21%)      | 40 / 123 (32.52%) | 5 / 6 (83.33%)     |
| number of deaths (all causes)                                       | 82                     | 40                | 5                  |
| number of deaths resulting from adverse events                      |                        |                   |                    |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                        |                   |                    |
| Metastases to central nervous system                                |                        |                   |                    |

|  |                   |                 |                |
|--|-------------------|-----------------|----------------|
| subjects affected / exposed                          | 0 / 113 (0.00%)   | 0 / 123 (0.00%) | 0 / 6 (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          |
| Malignant neoplasm progression                       |                   |                 |                |
| subjects affected / exposed                          | 24 / 113 (21.24%) | 2 / 123 (1.63%) | 3 / 6 (50.00%) |
| occurrences causally related to treatment / all      | 0 / 26            | 0 / 2           | 0 / 3          |
| deaths causally related to treatment / all           | 0 / 19            | 0 / 2           | 0 / 3          |
| Acute myeloid leukaemia                              |                   |                 |                |
| subjects affected / exposed                          | 1 / 113 (0.88%)   | 0 / 123 (0.00%) | 0 / 6 (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          |
| Extranodal marginal zone B-cell lymphoma (MALT type) |                   |                 |                |
| subjects affected / exposed                          | 0 / 113 (0.00%)   | 1 / 123 (0.81%) | 0 / 6 (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          |
| Infected neoplasm                                    |                   |                 |                |
| subjects affected / exposed                          | 0 / 113 (0.00%)   | 0 / 123 (0.00%) | 0 / 6 (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          |
| Lung adenocarcinoma                                  |                   |                 |                |
| subjects affected / exposed                          | 0 / 113 (0.00%)   | 0 / 123 (0.00%) | 0 / 6 (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          |
| Lung neoplasm malignant                              |                   |                 |                |
| subjects affected / exposed                          | 1 / 113 (0.88%)   | 0 / 123 (0.00%) | 0 / 6 (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 melanoma                                   |                   |                 |                |
| subjects affected / exposed                          | 0 / 113 (0.00%)   | 1 / 123 (0.81%) | 0 / 6 (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          |
| Tumour obstruction                                   |                   |                 |                |

|   |                 |                 |                |
|---|-----------------|-----------------|----------------|
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 1 / 6 (16.67%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0          |
| Tumour haemorrhage                              |                 |                 |                |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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          |
| Transitional cell carcinoma                     |                 |                 |                |
| subjects affected / exposed                     | 1 / 113 (0.88%) | 0 / 123 (0.00%) | 0 / 6 (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          |
| Squamous cell carcinoma of skin                 |                 |                 |                |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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          |
| Prostate cancer                                 |                 |                 |                |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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          |
| Neuroendocrine carcinoma of the skin            |                 |                 |                |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 1 / 123 (0.81%) | 0 / 6 (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          |
| Metastasis                                      |                 |                 |                |
| subjects affected / exposed                     | 2 / 113 (1.77%) | 0 / 123 (0.00%) | 0 / 6 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 3           | 0 / 0           | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0          |
| Tumour pain                                     |                 |                 |                |
| subjects affected / exposed                     | 1 / 113 (0.88%) | 0 / 123 (0.00%) | 0 / 6 (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          |
| Vascular disorders                              |                 |                 |                |
| Arterial haemorrhage                            |                 |                 |                |



|   |                 |                 |                |
|---|-----------------|-----------------|----------------|
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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          |
| Deep vein thrombosis                            |                 |                 |                |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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          |
| Embolism  |                 |                 |                |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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          |
| Haematoma                                       |                 |                 |                |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 1 / 123 (0.81%) | 0 / 6 (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          |
| Hypotension                                     |                 |                 |                |
| subjects affected / exposed                     | 2 / 113 (1.77%) | 0 / 123 (0.00%) | 1 / 6 (16.67%) |
| occurrences causally related to treatment / all | 1 / 3           | 0 / 0           | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0          |
| Orthostatic hypotension                         |                 |                 |                |
| subjects affected / exposed                     | 1 / 113 (0.88%) | 0 / 123 (0.00%) | 0 / 6 (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          |
| Lymphoedema                                     |                 |                 |                |
| subjects affected / exposed                     | 1 / 113 (0.88%) | 0 / 123 (0.00%) | 0 / 6 (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          |
| Iliac vein stenosis                             |                 |                 |                |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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          |
| Surgical and medical procedures                 |                 |                 |                |
| Debridement                                     |                 |                 |                |

|  |                 |                 |               |
|--|-----------------|-----------------|---------------|
| subjects affected / exposed                          | 0 / 113 (0.00%) | 1 / 123 (0.81%) | 0 / 6 (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         |
| General disorders and administration site conditions |                 |                 |               |
| Asthenia   |                 |                 |               |
| subjects affected / exposed                          | 1 / 113 (0.88%) | 1 / 123 (0.81%) | 0 / 6 (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         |
| Chills   |                 |                 |               |
| subjects affected / exposed                          | 0 / 113 (0.00%) | 1 / 123 (0.81%) | 0 / 6 (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         |
| Facial pain  |                 |                 |               |
| subjects affected / exposed                          | 0 / 113 (0.00%) | 1 / 123 (0.81%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0           | 1 / 3           | 0 / 0         |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           | 0 / 0         |
| Fatigue  |                 |                 |               |
| subjects affected / exposed                          | 0 / 113 (0.00%) | 1 / 123 (0.81%) | 0 / 6 (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         |
| General physical health deterioration                |                 |                 |               |
| subjects affected / exposed                          | 1 / 113 (0.88%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Disease progression                                  |                 |                 |               |
| subjects affected / exposed                          | 1 / 113 (0.88%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Death  |                 |                 |               |
| subjects affected / exposed                          | 1 / 113 (0.88%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Complication associated with device                  |                 |                 |               |

|   |                 |                 |               |
|---|-----------------|-----------------|---------------|
| subjects affected / exposed                     | 1 / 113 (0.88%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Hyperthermia                                    |                 |                 |               |
| subjects affected / exposed                     | 1 / 113 (0.88%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Malaise   |                 |                 |               |
| subjects affected / exposed                     | 2 / 113 (1.77%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Non-cardiac chest pain                          |                 |                 |               |
| subjects affected / exposed                     | 1 / 113 (0.88%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Multiple organ dysfunction syndrome             |                 |                 |               |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 1 / 123 (0.81%) | 0 / 6 (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         |
| Mucosal inflammation                            |                 |                 |               |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 3 / 123 (2.44%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 3           | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0         |
| Oedema peripheral                               |                 |                 |               |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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                     | 0 / 113 (0.00%) | 1 / 123 (0.81%) | 0 / 6 (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         |
| Sudden death                                    |                 |                 |               |

|   |                 |                 |               |
|---|-----------------|-----------------|---------------|
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Pyrexia   |                 |                 |               |
| subjects affected / exposed                     | 3 / 113 (2.65%) | 2 / 123 (1.63%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 1 / 3           | 1 / 3           | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0         |
| Performance status decreased                    |                 |                 |               |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Pain  |                 |                 |               |
| subjects affected / exposed                     | 1 / 113 (0.88%) | 1 / 123 (0.81%) | 0 / 6 (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         |
| Immune system disorders                         |                 |                 |               |
| Anaphylactic reaction                           |                 |                 |               |
| subjects affected / exposed                     | 1 / 113 (0.88%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Hypersensitivity                                |                 |                 |               |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Sarcoidosis                                     |                 |                 |               |
| subjects affected / exposed                     | 1 / 113 (0.88%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Reproductive system and breast disorders        |                 |                 |               |
| Vaginal haemorrhage                             |                 |                 |               |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 1 / 123 (0.81%) | 0 / 6 (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         |

|   |                 |                 |               |
|---|-----------------|-----------------|---------------|
| Prostatic obstruction                           |                 |                 |               |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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 pain                                     |                 |                 |               |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Female genital tract fistula                    |                 |                 |               |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Vulval disorder                                 |                 |                 |               |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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 |                 |                 |               |
| Acute respiratory distress syndrome             |                 |                 |               |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Aspiration                                      |                 |                 |               |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 2 / 123 (1.63%) | 0 / 6 (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         |
| Hypoxia   |                 |                 |               |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 1 / 123 (0.81%) | 0 / 6 (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         |
| Haemoptysis                                     |                 |                 |               |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 1 / 123 (0.81%) | 0 / 6 (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         |

|   |                 |                 |               |
|---|-----------------|-----------------|---------------|
| Dyspnoea  |                 |                 |               |
| subjects affected / exposed                     | 4 / 113 (3.54%) | 0 / 123 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 4           | 0 / 0           | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0         |
| Asthma  |                 |                 |               |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Immune-mediated lung disease                    |                 |                 |               |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Pleural effusion                                |                 |                 |               |
| subjects affected / exposed                     | 1 / 113 (0.88%) | 0 / 123 (0.00%) | 0 / 6 (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 disorder                                   |                 |                 |               |
| subjects affected / exposed                     | 1 / 113 (0.88%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Laryngeal oedema                                |                 |                 |               |
| subjects affected / exposed                     | 1 / 113 (0.88%) | 0 / 123 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 1 / 2           | 0 / 0           | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0         |
| Stridor   |                 |                 |               |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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                     | 1 / 113 (0.88%) | 1 / 123 (0.81%) | 0 / 6 (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         |
| Pneumonitis                                     |                 |                 |               |
| subjects affected / exposed                     | 4 / 113 (3.54%) | 0 / 123 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 4 / 4           | 0 / 0           | 0 / 0         |
| deaths causally related to treatment / all      | 1 / 1           | 0 / 0           | 0 / 0         |
| Pneumothorax                                    |                 |                 |               |
| subjects affected / exposed                     | 1 / 113 (0.88%) | 1 / 123 (0.81%) | 0 / 6 (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         |
| Productive cough                                |                 |                 |               |
| subjects affected / exposed                     | 1 / 113 (0.88%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Psychiatric disorders                           |                 |                 |               |
| Mental status changes                           |                 |                 |               |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Confusional state                               |                 |                 |               |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Product issues                                  |                 |                 |               |
| Device occlusion                                |                 |                 |               |
| subjects affected / exposed                     | 1 / 113 (0.88%) | 0 / 123 (0.00%) | 0 / 6 (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                                  |                 |                 |               |
| Alanine aminotransferase increased              |                 |                 |               |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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         |

|  |                 |                 |               |
|--|-----------------|-----------------|---------------|
| General physical condition abnormal<br>subjects affected / exposed | 0 / 113 (0.00%) | 1 / 123 (0.81%) | 0 / 6 (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         |
| Aspartate aminotransferase<br>increased                            |                 |                 |               |
| subjects affected / exposed  | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Blood bilirubin increased  |                 |                 |               |
| subjects affected / exposed  | 1 / 113 (0.88%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Blood creatinine increased   |                 |                 |               |
| subjects affected / exposed  | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Blood magnesium decreased  |                 |                 |               |
| subjects affected / exposed  | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Blood pressure decreased   |                 |                 |               |
| subjects affected / exposed  | 1 / 113 (0.88%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Cytomegalovirus test positive                                      |                 |                 |               |
| subjects affected / exposed  | 1 / 113 (0.88%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| International normalised ratio<br>increased                        |                 |                 |               |
| subjects affected / exposed  | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Liver function test increased                                      |                 |                 |               |



|   |                 |                 |               |
|---|-----------------|-----------------|---------------|
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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 syncytial virus test positive       |                 |                 |               |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Troponin I increased                            |                 |                 |               |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 1 / 123 (0.81%) | 0 / 6 (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         |
| Troponin increased                              |                 |                 |               |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Urine output decreased                          |                 |                 |               |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Lipase increased                                |                 |                 |               |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Injury, poisoning and procedural complications  |                 |                 |               |
| Fracture  |                 |                 |               |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Hip fracture                                    |                 |                 |               |
| subjects affected / exposed                     | 1 / 113 (0.88%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Post procedural fistula                         |                 |                 |               |

|   |                 |                 |               |
|---|-----------------|-----------------|---------------|
| subjects affected / exposed                     | 0 / 113 (0.00%) | 1 / 123 (0.81%) | 0 / 6 (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         |
| Transfusion reaction                            |                 |                 |               |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Post procedural haemorrhage                     |                 |                 |               |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 1 / 123 (0.81%) | 0 / 6 (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         |
| Postoperative wound complication                |                 |                 |               |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 1 / 123 (0.81%) | 0 / 6 (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         |
| Procedural pain                                 |                 |                 |               |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Recall phenomenon                               |                 |                 |               |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Spinal compression fracture                     |                 |                 |               |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Cardiac disorders                               |                 |                 |               |
| Acute coronary syndrome                         |                 |                 |               |

|   |                 |                 |               |
|---|-----------------|-----------------|---------------|
| subjects affected / exposed                     | 0 / 113 (0.00%) | 1 / 123 (0.81%) | 0 / 6 (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         |
| Cardiac failure                                 |                 |                 |               |
| subjects affected / exposed                     | 2 / 113 (1.77%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Cardiac tamponade                               |                 |                 |               |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Cardiac arrest                                  |                 |                 |               |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Autoimmune pericarditis                         |                 |                 |               |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Atrial fibrillation                             |                 |                 |               |
| subjects affected / exposed                     | 1 / 113 (0.88%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Coronary artery disease                         |                 |                 |               |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 1 / 123 (0.81%) | 0 / 6 (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         |
| Acute myocardial infarction                     |                 |                 |               |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 1 / 123 (0.81%) | 0 / 6 (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         |
| Angina pectoris                                 |                 |                 |               |

|   |                 |                 |               |
|---|-----------------|-----------------|---------------|
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Mitral valve incompetence                       |                 |                 |               |
| subjects affected / exposed                     | 1 / 113 (0.88%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Supraventricular tachycardia                    |                 |                 |               |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Sinus bradycardia                               |                 |                 |               |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Pericardial effusion                            |                 |                 |               |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Myocarditis                                     |                 |                 |               |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Myocardial infarction                           |                 |                 |               |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Nervous system disorders                        |                 |                 |               |
| Cerebrovascular accident                        |                 |                 |               |
| subjects affected / exposed                     | 1 / 113 (0.88%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Cerebral ischaemia                              |                 |                 |               |

|   |                 |                 |               |
|---|-----------------|-----------------|---------------|
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Cerebral infarction                             |                 |                 |               |
| subjects affected / exposed                     | 1 / 113 (0.88%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Cerebral haemorrhage                            |                 |                 |               |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Carotid artery aneurysm                         |                 |                 |               |
| subjects affected / exposed                     | 1 / 113 (0.88%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Bell's palsy                                    |                 |                 |               |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Basal ganglia infarction                        |                 |                 |               |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 1 / 123 (0.81%) | 0 / 6 (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         |
| Headache  |                 |                 |               |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Haemorrhage intracranial                        |                 |                 |               |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Guillain-Barre syndrome                         |                 |                 |               |

|   |                 |                 |               |
|---|-----------------|-----------------|---------------|
| subjects affected / exposed                     | 1 / 113 (0.88%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Encephalopathy                                  |                 |                 |               |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Embolic stroke                                  |                 |                 |               |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Dizziness                                       |                 |                 |               |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Depressed level of consciousness                |                 |                 |               |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Intraventricular haemorrhage                    |                 |                 |               |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Syncope   |                 |                 |               |
| subjects affected / exposed                     | 1 / 113 (0.88%) | 1 / 123 (0.81%) | 0 / 6 (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         |
| Spinal cord compression                         |                 |                 |               |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Seizure   |                 |                 |               |

|   |                 |                 |               |
|---|-----------------|-----------------|---------------|
| subjects affected / exposed                     | 0 / 113 (0.00%) | 1 / 123 (0.81%) | 0 / 6 (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         |
| Peripheral sensory neuropathy                   |                 |                 |               |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Peripheral motor neuropathy                     |                 |                 |               |
| subjects affected / exposed                     | 1 / 113 (0.88%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Myasthenia gravis                               |                 |                 |               |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 1 / 123 (0.81%) | 0 / 6 (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         |
| Monoparesis                                     |                 |                 |               |
| subjects affected / exposed                     | 1 / 113 (0.88%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Blood and lymphatic system disorders            |                 |                 |               |
| Febrile neutropenia                             |                 |                 |               |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 2 / 123 (1.63%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 2           | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 1           | 0 / 0         |
| Anaemia   |                 |                 |               |
| subjects affected / exposed                     | 1 / 113 (0.88%) | 1 / 123 (0.81%) | 0 / 6 (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         |
| Lymph node pain                                 |                 |                 |               |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Iron deficiency anaemia                         |                 |                 |               |

|   |                 |                 |               |
|---|-----------------|-----------------|---------------|
| subjects affected / exposed                     | 1 / 113 (0.88%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Eye disorders                                   |                 |                 |               |
| Uveitis   |                 |                 |               |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Gastrointestinal disorders                      |                 |                 |               |
| Abdominal distension                            |                 |                 |               |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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                     | 0 / 113 (0.00%) | 1 / 123 (0.81%) | 0 / 6 (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         |
| Constipation                                    |                 |                 |               |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Colitis   |                 |                 |               |
| subjects affected / exposed                     | 1 / 113 (0.88%) | 1 / 123 (0.81%) | 0 / 6 (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         |
| Ascites   |                 |                 |               |
| subjects affected / exposed                     | 1 / 113 (0.88%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Anorectal disorder                              |                 |                 |               |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Anal fistula                                    |                 |                 |               |



|   |                 |                 |               |
|---|-----------------|-----------------|---------------|
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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 lower                            |                 |                 |               |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 1 / 123 (0.81%) | 0 / 6 (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         |
| Gastritis                                       |                 |                 |               |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Dysphagia                                       |                 |                 |               |
| subjects affected / exposed                     | 1 / 113 (0.88%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Diarrhoea                                       |                 |                 |               |
| subjects affected / exposed                     | 1 / 113 (0.88%) | 2 / 123 (1.63%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1           | 1 / 2           | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0         |
| Gastrointestinal haemorrhage                    |                 |                 |               |
| subjects affected / exposed                     | 1 / 113 (0.88%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Gastrointestinal motility disorder              |                 |                 |               |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Glossodynia                                     |                 |                 |               |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 1 / 123 (0.81%) | 0 / 6 (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         |
| Ileus   |                 |                 |               |

|   |                 |                 |               |
|---|-----------------|-----------------|---------------|
| subjects affected / exposed                     | 0 / 113 (0.00%) | 1 / 123 (0.81%) | 0 / 6 (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         |
| Immune-mediated enterocolitis                   |                 |                 |               |
| subjects affected / exposed                     | 1 / 113 (0.88%) | 1 / 123 (0.81%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1           | 1 / 1           | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0         |
| Intestinal perforation                          |                 |                 |               |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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 obstruction                          |                 |                 |               |
| subjects affected / exposed                     | 1 / 113 (0.88%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Immune-mediated pancreatitis                    |                 |                 |               |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Large intestinal obstruction                    |                 |                 |               |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Oesophagitis                                    |                 |                 |               |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Oesophageal motility disorder                   |                 |                 |               |
| subjects affected / exposed                     | 1 / 113 (0.88%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Nausea  |                 |                 |               |

|   |                 |                 |               |
|---|-----------------|-----------------|---------------|
| subjects affected / exposed                     | 0 / 113 (0.00%) | 1 / 123 (0.81%) | 0 / 6 (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         |
| Mouth haemorrhage                               |                 |                 |               |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 3 / 123 (2.44%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 2 / 3           | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0         |
| Vomiting  |                 |                 |               |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 1 / 123 (0.81%) | 0 / 6 (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         |
| Pancreatitis                                    |                 |                 |               |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 1 / 123 (0.81%) | 0 / 6 (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         |
| Proctalgia                                      |                 |                 |               |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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 / 113 (1.77%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Stomatitis                                      |                 |                 |               |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Hepatobiliary disorders                         |                 |                 |               |
| Autoimmune cholangitis                          |                 |                 |               |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Cholecystitis                                   |                 |                 |               |

|   |                 |                 |               |
|---|-----------------|-----------------|---------------|
| subjects affected / exposed                     | 1 / 113 (0.88%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Biliary tract disorder                          |                 |                 |               |
| subjects affected / exposed                     | 1 / 113 (0.88%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Biliary obstruction                             |                 |                 |               |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Bile duct stenosis                              |                 |                 |               |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Autoimmune hepatitis                            |                 |                 |               |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Gallbladder rupture                             |                 |                 |               |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Hypertransaminaemia                             |                 |                 |               |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Hepatotoxicity                                  |                 |                 |               |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Hepatitis toxic                                 |                 |                 |               |

|   |                 |                 |               |
|---|-----------------|-----------------|---------------|
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Hepatitis                                       |                 |                 |               |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Hepatic function abnormal                       |                 |                 |               |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Hepatic cytolysis                               |                 |                 |               |
| subjects affected / exposed                     | 2 / 113 (1.77%) | 0 / 123 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 1 / 2           | 0 / 0           | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0         |
| Skin and subcutaneous tissue disorders          |                 |                 |               |
| Hyperhidrosis                                   |                 |                 |               |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 1 / 123 (0.81%) | 0 / 6 (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         |
| Rash  |                 |                 |               |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Rash maculo-papular                             |                 |                 |               |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Rash pruritic                                   |                 |                 |               |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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 and urinary disorders                     |                 |                 |               |

|   |                 |                 |               |
|---|-----------------|-----------------|---------------|
| Hydronephrosis                                  |                 |                 |               |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Haematuria                                      |                 |                 |               |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Autoimmune nephritis                            |                 |                 |               |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Acute kidney injury                             |                 |                 |               |
| subjects affected / exposed                     | 2 / 113 (1.77%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Oliguria  |                 |                 |               |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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 colic                                     |                 |                 |               |
| subjects affected / exposed                     | 1 / 113 (0.88%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Urogenital fistula                              |                 |                 |               |
| subjects affected / exposed                     | 1 / 113 (0.88%) | 0 / 123 (0.00%) | 0 / 6 (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 obstruction                       |                 |                 |               |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Urinary retention                               |                 |                 |               |

|   |                 |                 |               |
|---|-----------------|-----------------|---------------|
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Urinary incontinence                            |                 |                 |               |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Ureteric stenosis                               |                 |                 |               |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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 haematoma                                 |                 |                 |               |
| subjects affected / exposed                     | 1 / 113 (0.88%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Renal failure                                   |                 |                 |               |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Endocrine disorders                             |                 |                 |               |
| Adrenal insufficiency                           |                 |                 |               |
| subjects affected / exposed                     | 1 / 113 (0.88%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Glucocorticoid deficiency                       |                 |                 |               |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Thyroid disorder                                |                 |                 |               |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Inappropriate antidiuretic hormone secretion    |                 |                 |               |

|   |                 |                 |               |
|---|-----------------|-----------------|---------------|
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Hypothyroidism                                  |                 |                 |               |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Hypophysitis                                    |                 |                 |               |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Hyperthyroidism                                 |                 |                 |               |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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 |                 |                 |               |
| Pain in extremity                               |                 |                 |               |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Myositis  |                 |                 |               |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Muscular weakness                               |                 |                 |               |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 1 / 123 (0.81%) | 0 / 6 (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         |
| Intervertebral disc protrusion                  |                 |                 |               |
| subjects affected / exposed                     | 1 / 113 (0.88%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Flank pain                                      |                 |                 |               |



|   |                 |                 |               |
|---|-----------------|-----------------|---------------|
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Fistula   |                 |                 |               |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Back pain                                       |                 |                 |               |
| subjects affected / exposed                     | 1 / 113 (0.88%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Arthralgia                                      |                 |                 |               |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Pathological fracture                           |                 |                 |               |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Infections and infestations                     |                 |                 |               |
| Cellulitis                                      |                 |                 |               |
| subjects affected / exposed                     | 1 / 113 (0.88%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Catheter site infection                         |                 |                 |               |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Bacteraemia                                     |                 |                 |               |

|   |                 |                 |               |
|---|-----------------|-----------------|---------------|
| subjects affected / exposed                     | 1 / 113 (0.88%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Arthritis bacterial                             |                 |                 |               |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Abscess neck                                    |                 |                 |               |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 1 / 123 (0.81%) | 0 / 6 (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         |
| Gastroenteritis                                 |                 |                 |               |
| subjects affected / exposed                     | 1 / 113 (0.88%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Encephalitis                                    |                 |                 |               |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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 sepsis                           |                 |                 |               |
| subjects affected / exposed                     | 1 / 113 (0.88%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Device related infection                        |                 |                 |               |
| subjects affected / exposed                     | 2 / 113 (1.77%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Clostridium difficile colitis                   |                 |                 |               |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 1 / 123 (0.81%) | 0 / 6 (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         |
| Clostridial sepsis                              |                 |                 |               |

|   |                 |                 |               |
|---|-----------------|-----------------|---------------|
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Gastroenteritis bacterial                       |                 |                 |               |
| subjects affected / exposed                     | 1 / 113 (0.88%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Kidney infection                                |                 |                 |               |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Osteomyelitis                                   |                 |                 |               |
| subjects affected / exposed                     | 1 / 113 (0.88%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Meningitis aseptic                              |                 |                 |               |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Meningitis                                      |                 |                 |               |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Medical device site infection                   |                 |                 |               |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 1 / 123 (0.81%) | 0 / 6 (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         |
| Lower respiratory tract infection               |                 |                 |               |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Localised infection                             |                 |                 |               |

|   |                 |                 |                |
|---|-----------------|-----------------|----------------|
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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          |
| Large intestine infection                       |                 |                 |                |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 1 / 6 (16.67%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0          |
| Postoperative wound infection                   |                 |                 |                |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 1 / 123 (0.81%) | 0 / 6 (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          |
| Post procedural infection                       |                 |                 |                |
| subjects affected / exposed                     | 1 / 113 (0.88%) | 0 / 123 (0.00%) | 0 / 6 (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 bacterial                             |                 |                 |                |
| subjects affected / exposed                     | 1 / 113 (0.88%) | 0 / 123 (0.00%) | 0 / 6 (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 aspiration                            |                 |                 |                |
| subjects affected / exposed                     | 1 / 113 (0.88%) | 1 / 123 (0.81%) | 0 / 6 (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          |
| Pneumonia                                       |                 |                 |                |
| subjects affected / exposed                     | 2 / 113 (1.77%) | 0 / 123 (0.00%) | 1 / 6 (16.67%) |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 0           | 0 / 2          |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0          |
| Periorbital infection                           |                 |                 |                |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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          |
| Otitis media                                    |                 |                 |                |

|   |                 |                 |                |
|---|-----------------|-----------------|----------------|
| subjects affected / exposed                     | 1 / 113 (0.88%) | 0 / 123 (0.00%) | 0 / 6 (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          |
| Pulmonary sepsis                                |                 |                 |                |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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 tract infection                     |                 |                 |                |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 1 / 6 (16.67%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0          |
| Sepsis  |                 |                 |                |
| subjects affected / exposed                     | 3 / 113 (2.65%) | 1 / 123 (0.81%) | 0 / 6 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 3           | 0 / 1           | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 2           | 0 / 0           | 0 / 0          |
| Septic shock                                    |                 |                 |                |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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          |
| Sinusitis                                       |                 |                 |                |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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          |
| Skin infection                                  |                 |                 |                |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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          |
| Soft tissue infection                           |                 |                 |                |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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 / 113 (0.88%) | 0 / 123 (0.00%) | 0 / 6 (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                     | 0 / 113 (0.00%) | 1 / 123 (0.81%) | 0 / 6 (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         |
| Tuberculosis                                    |                 |                 |               |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Upper respiratory tract infection               |                 |                 |               |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Urinary tract infection                         |                 |                 |               |
| subjects affected / exposed                     | 3 / 113 (2.65%) | 0 / 123 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 3           | 0 / 0           | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0         |
| Urosepsis                                       |                 |                 |               |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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 device infection                       |                 |                 |               |
| subjects affected / exposed                     | 1 / 113 (0.88%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Metabolism and nutrition disorders              |                 |                 |               |
| Decreased appetite                              |                 |                 |               |
| subjects affected / exposed                     | 1 / 113 (0.88%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Dehydration                                     |                 |                 |               |

|   |                 |                 |               |
|---|-----------------|-----------------|---------------|
| subjects affected / exposed                     | 1 / 113 (0.88%) | 3 / 123 (2.44%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 2 / 3           | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0         |
| Hypercalcaemia                                  |                 |                 |               |
| subjects affected / exposed                     | 1 / 113 (0.88%) | 1 / 123 (0.81%) | 0 / 6 (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         |
| Hyperglycaemia                                  |                 |                 |               |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Hyperkalaemia                                   |                 |                 |               |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Hypokalaemia                                    |                 |                 |               |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Hyponatraemia                                   |                 |                 |               |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Hypophagia                                      |                 |                 |               |
| subjects affected / exposed                     | 1 / 113 (0.88%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Type 1 diabetes mellitus                        |                 |                 |               |
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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         |
| Diabetic ketoacidosis                           |                 |                 |               |

|   |                 |                 |               |
|---|-----------------|-----------------|---------------|
| subjects affected / exposed                     | 0 / 113 (0.00%) | 0 / 123 (0.00%) | 0 / 6 (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>Serious adverse events</b>                                       | Metastatic Combo B | Metastatic Combo C | Metastatic Combo A |
|---|--------------------|--------------------|--------------------|
| Total subjects affected by serious adverse events                   |                    |                    |                    |
| subjects affected / exposed   | 99 / 133 (74.44%)  | 5 / 8 (62.50%)     | 130 / 195 (66.67%) |
| number of deaths (all causes)                                       | 86                 | 7                  | 133                |
| number of deaths resulting from adverse events                      |                    |                    |                    |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                    |                    |                    |
| Metastases to central nervous system                                |                    |                    |                    |
| subjects affected / exposed   | 0 / 133 (0.00%)    | 0 / 8 (0.00%)      | 1 / 195 (0.51%)    |
| occurrences causally related to treatment / all                     | 0 / 0              | 0 / 0              | 0 / 1              |
| deaths causally related to treatment / all                          | 0 / 0              | 0 / 0              | 0 / 0              |
| Malignant neoplasm progression                                      |                    |                    |                    |
| subjects affected / exposed   | 21 / 133 (15.79%)  | 2 / 8 (25.00%)     | 39 / 195 (20.00%)  |
| occurrences causally related to treatment / all                     | 0 / 21             | 0 / 2              | 0 / 40             |
| deaths causally related to treatment / all                          | 0 / 20             | 0 / 2              | 0 / 34             |
| Acute myeloid leukaemia   |                    |                    |                    |
| subjects affected / exposed   | 0 / 133 (0.00%)    | 0 / 8 (0.00%)      | 0 / 195 (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              |
| Extranodal marginal zone B-cell lymphoma (MALT type)                |                    |                    |                    |
| subjects affected / exposed   | 0 / 133 (0.00%)    | 0 / 8 (0.00%)      | 0 / 195 (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              |
| Infected neoplasm   |                    |                    |                    |
| subjects affected / exposed   | 2 / 133 (1.50%)    | 0 / 8 (0.00%)      | 1 / 195 (0.51%)    |
| occurrences causally related to treatment / all                     | 0 / 2              | 0 / 0              | 0 / 1              |
| deaths causally related to treatment / all                          | 0 / 0              | 0 / 0              | 0 / 1              |
| Lung adenocarcinoma   |                    |                    |                    |



|   |                 |               |                 |
|---|-----------------|---------------|-----------------|
| subjects affected / exposed                     | 1 / 133 (0.75%) | 0 / 8 (0.00%) | 0 / 195 (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 neoplasm malignant                         |                 |               |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 0 / 195 (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           |
| Malignant melanoma                              |                 |               |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 0 / 195 (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 obstruction                              |                 |               |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 0 / 195 (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 haemorrhage                              |                 |               |                 |
| subjects affected / exposed                     | 1 / 133 (0.75%) | 0 / 8 (0.00%) | 1 / 195 (0.51%) |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 0         | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 0           |
| Transitional cell carcinoma                     |                 |               |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 0 / 195 (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           |
| Squamous cell carcinoma of skin                 |                 |               |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 1 / 195 (0.51%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 0           |
| Prostate cancer                                 |                 |               |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 1 / 195 (0.51%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 0           |
| Neuroendocrine carcinoma of the skin            |                 |               |                 |

|   |                 |               |                 |
|---|-----------------|---------------|-----------------|
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 0 / 195 (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           |
| Metastasis                                      |                 |               |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 0 / 195 (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                     | 1 / 133 (0.75%) | 0 / 8 (0.00%) | 0 / 195 (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           |
| Vascular disorders                              |                 |               |                 |
| Arterial haemorrhage                            |                 |               |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 1 / 195 (0.51%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 0           |
| Deep vein thrombosis                            |                 |               |                 |
| subjects affected / exposed                     | 1 / 133 (0.75%) | 0 / 8 (0.00%) | 2 / 195 (1.03%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0         | 0 / 2           |
| deaths causally related to treatment / all      | 0 / 1           | 0 / 0         | 0 / 0           |
| Embolism  |                 |               |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 1 / 195 (0.51%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 0           |
| Haematoma                                       |                 |               |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 0 / 195 (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           |
| Hypotension                                     |                 |               |                 |
| subjects affected / exposed                     | 1 / 133 (0.75%) | 0 / 8 (0.00%) | 1 / 195 (0.51%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0         | 0 / 2           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 0           |
| Orthostatic hypotension                         |                 |               |                 |

|  |                 |               |                 |
|--|-----------------|---------------|-----------------|
| subjects affected / exposed                          | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 0 / 195 (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           |
| Lymphoedema  |                 |               |                 |
| subjects affected / exposed                          | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 0 / 195 (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           |
| Iliac vein stenosis                                  |                 |               |                 |
| subjects affected / exposed                          | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 1 / 195 (0.51%) |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 1           |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0         | 0 / 0           |
| Surgical and medical procedures                      |                 |               |                 |
| Debridement  |                 |               |                 |
| subjects affected / exposed                          | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 0 / 195 (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           |
| General disorders and administration site conditions |                 |               |                 |
| Asthenia   |                 |               |                 |
| subjects affected / exposed                          | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 1 / 195 (0.51%) |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 1           |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0         | 0 / 1           |
| Chills   |                 |               |                 |
| subjects affected / exposed                          | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 0 / 195 (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           |
| Facial pain  |                 |               |                 |
| subjects affected / exposed                          | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 0 / 195 (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           |
| Fatigue  |                 |               |                 |
| subjects affected / exposed                          | 1 / 133 (0.75%) | 0 / 8 (0.00%) | 1 / 195 (0.51%) |
| occurrences causally related to treatment / all      | 1 / 1           | 0 / 0         | 1 / 1           |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0         | 0 / 0           |

|   |                 |               |                 |
|---|-----------------|---------------|-----------------|
| General physical health deterioration           |                 |               |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 0 / 195 (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                     | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 1 / 195 (0.51%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 1           |
| Death   |                 |               |                 |
| subjects affected / exposed                     | 1 / 133 (0.75%) | 0 / 8 (0.00%) | 2 / 195 (1.03%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0         | 0 / 2           |
| deaths causally related to treatment / all      | 0 / 1           | 0 / 0         | 0 / 2           |
| Complication associated with device             |                 |               |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 0 / 195 (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           |
| Hyperthermia                                    |                 |               |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 0 / 195 (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           |
| Malaise   |                 |               |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 0 / 195 (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           |
| Non-cardiac chest pain                          |                 |               |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 0 / 195 (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           |
| Multiple organ dysfunction syndrome             |                 |               |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 0 / 195 (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           |
| Mucosal inflammation                            |                 |               |                 |

|   |                 |               |                 |
|---|-----------------|---------------|-----------------|
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 0 / 195 (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           |
| Oedema peripheral                               |                 |               |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 2 / 195 (1.03%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         | 1 / 2           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 0           |
| Systemic inflammatory response syndrome         |                 |               |                 |
| subjects affected / exposed                     | 1 / 133 (0.75%) | 0 / 8 (0.00%) | 0 / 195 (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           |
| Sudden death                                    |                 |               |                 |
| subjects affected / exposed                     | 1 / 133 (0.75%) | 0 / 8 (0.00%) | 0 / 195 (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           |
| Pyrexia   |                 |               |                 |
| subjects affected / exposed                     | 7 / 133 (5.26%) | 0 / 8 (0.00%) | 5 / 195 (2.56%) |
| occurrences causally related to treatment / all | 3 / 9           | 0 / 0         | 1 / 5           |
| deaths causally related to treatment / all      | 0 / 1           | 0 / 0         | 0 / 0           |
| Performance status decreased                    |                 |               |                 |
| subjects affected / exposed                     | 1 / 133 (0.75%) | 0 / 8 (0.00%) | 0 / 195 (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           |
| Pain  |                 |               |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 2 / 195 (1.03%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         | 0 / 2           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 0           |
| Immune system disorders                         |                 |               |                 |
| Anaphylactic reaction                           |                 |               |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 0 / 195 (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           |
| Hypersensitivity                                |                 |               |                 |

|   |                 |               |                 |
|---|-----------------|---------------|-----------------|
| subjects affected / exposed                     | 1 / 133 (0.75%) | 0 / 8 (0.00%) | 1 / 195 (0.51%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0         | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 0           |
| Sarcoidosis                                     |                 |               |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 0 / 195 (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           |
| Reproductive system and breast disorders        |                 |               |                 |
| Vaginal haemorrhage                             |                 |               |                 |
| subjects affected / exposed                     | 2 / 133 (1.50%) | 0 / 8 (0.00%) | 0 / 195 (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           |
| Prostatic obstruction                           |                 |               |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 1 / 195 (0.51%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 0           |
| Pelvic pain                                     |                 |               |                 |
| subjects affected / exposed                     | 1 / 133 (0.75%) | 0 / 8 (0.00%) | 1 / 195 (0.51%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0         | 0 / 2           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 0           |
| Female genital tract fistula                    |                 |               |                 |
| subjects affected / exposed                     | 2 / 133 (1.50%) | 0 / 8 (0.00%) | 1 / 195 (0.51%) |
| occurrences causally related to treatment / all | 1 / 2           | 0 / 0         | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 0           |
| Vulval disorder                                 |                 |               |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 1 / 195 (0.51%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 0           |
| Respiratory, thoracic and mediastinal disorders |                 |               |                 |
| Acute respiratory distress syndrome             |                 |               |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 1 / 195 (0.51%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 0           |

|   |                 |                |                 |
|---|-----------------|----------------|-----------------|
| Aspiration                                      |                 |                |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%)  | 3 / 195 (1.54%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 0 / 4           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 1           |
| Hypoxia   |                 |                |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%)  | 1 / 195 (0.51%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0           |
| Haemoptysis                                     |                 |                |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%)  | 0 / 195 (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           |
| Dyspnoea  |                 |                |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 2 / 8 (25.00%) | 2 / 195 (1.03%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 2          | 1 / 2           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0           |
| Asthma  |                 |                |                 |
| subjects affected / exposed                     | 1 / 133 (0.75%) | 0 / 8 (0.00%)  | 0 / 195 (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-mediated lung disease                    |                 |                |                 |
| subjects affected / exposed                     | 1 / 133 (0.75%) | 0 / 8 (0.00%)  | 0 / 195 (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           |
| Pleural effusion                                |                 |                |                 |
| subjects affected / exposed                     | 1 / 133 (0.75%) | 1 / 8 (12.50%) | 3 / 195 (1.54%) |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 1          | 0 / 3           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 1           |
| Lung disorder                                   |                 |                |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%)  | 0 / 195 (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           |
| Laryngeal oedema                                |                 |                |                 |

|   |                  |                |                 |
|---|------------------|----------------|-----------------|
| subjects affected / exposed                     | 0 / 133 (0.00%)  | 0 / 8 (0.00%)  | 0 / 195 (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           |
| Stridor   |                  |                |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%)  | 1 / 8 (12.50%) | 0 / 195 (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           |
| Pulmonary haemorrhage                           |                  |                |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%)  | 1 / 8 (12.50%) | 0 / 195 (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           |
| Pulmonary embolism                              |                  |                |                 |
| subjects affected / exposed                     | 2 / 133 (1.50%)  | 0 / 8 (0.00%)  | 2 / 195 (1.03%) |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0          | 0 / 3           |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0          | 0 / 0           |
| Pneumonitis                                     |                  |                |                 |
| subjects affected / exposed                     | 10 / 133 (7.52%) | 0 / 8 (0.00%)  | 7 / 195 (3.59%) |
| occurrences causally related to treatment / all | 10 / 10          | 0 / 0          | 7 / 7           |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0          | 0 / 0           |
| Pneumothorax                                    |                  |                |                 |
| subjects affected / exposed                     | 1 / 133 (0.75%)  | 0 / 8 (0.00%)  | 2 / 195 (1.03%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0          | 0 / 2           |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0          | 0 / 0           |
| Productive cough                                |                  |                |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%)  | 0 / 8 (0.00%)  | 0 / 195 (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                           |                  |                |                 |
| Mental status changes                           |                  |                |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%)  | 0 / 8 (0.00%)  | 1 / 195 (0.51%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0          | 0 / 2           |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0          | 0 / 0           |
| Confusional state                               |                  |                |                 |



|   |                 |               |                 |
|---|-----------------|---------------|-----------------|
| subjects affected / exposed                     | 1 / 133 (0.75%) | 0 / 8 (0.00%) | 3 / 195 (1.54%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0         | 0 / 3           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 0           |
| Product issues                                  |                 |               |                 |
| Device occlusion                                |                 |               |                 |
| subjects affected / exposed                     | 1 / 133 (0.75%) | 0 / 8 (0.00%) | 2 / 195 (1.03%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0         | 0 / 2           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 0           |
| Investigations                                  |                 |               |                 |
| Alanine aminotransferase increased              |                 |               |                 |
| subjects affected / exposed                     | 1 / 133 (0.75%) | 0 / 8 (0.00%) | 1 / 195 (0.51%) |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0         | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 0           |
| General physical condition abnormal             |                 |               |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 0 / 195 (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           |
| Aspartate aminotransferase increased            |                 |               |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 1 / 195 (0.51%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 0           |
| Blood bilirubin increased                       |                 |               |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 0 / 195 (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           |
| Blood creatinine increased                      |                 |               |                 |
| subjects affected / exposed                     | 1 / 133 (0.75%) | 0 / 8 (0.00%) | 1 / 195 (0.51%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0         | 0 / 2           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 0           |
| Blood magnesium decreased                       |                 |               |                 |
| subjects affected / exposed                     | 1 / 133 (0.75%) | 0 / 8 (0.00%) | 0 / 195 (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           |

|   |                 |               |                 |
|---|-----------------|---------------|-----------------|
| Blood pressure decreased                        |                 |               |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 0 / 195 (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 test positive                   |                 |               |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 0 / 195 (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           |
| International normalised ratio increased        |                 |               |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 1 / 195 (0.51%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 0           |
| Liver function test increased                   |                 |               |                 |
| subjects affected / exposed                     | 1 / 133 (0.75%) | 0 / 8 (0.00%) | 1 / 195 (0.51%) |
| occurrences causally related to treatment / all | 2 / 2           | 0 / 0         | 1 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 0           |
| Respiratory syncytial virus test positive       |                 |               |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 1 / 195 (0.51%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 0           |
| Troponin I increased                            |                 |               |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 0 / 195 (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           |
| Troponin increased                              |                 |               |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 1 / 195 (0.51%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 0           |
| Urine output decreased                          |                 |               |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 1 / 195 (0.51%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 0           |
| Lipase increased                                |                 |               |                 |

|   |                 |               |                 |
|---|-----------------|---------------|-----------------|
| subjects affected / exposed                     | 2 / 133 (1.50%) | 0 / 8 (0.00%) | 2 / 195 (1.03%) |
| occurrences causally related to treatment / all | 2 / 2           | 0 / 0         | 2 / 2           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 0           |
| Injury, poisoning and procedural complications  |                 |               |                 |
| Fracture  |                 |               |                 |
| subjects affected / exposed                     | 1 / 133 (0.75%) | 0 / 8 (0.00%) | 0 / 195 (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           |
| Hip fracture                                    |                 |               |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 0 / 195 (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           |
| Post procedural fistula                         |                 |               |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 0 / 195 (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           |
| Transfusion reaction                            |                 |               |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 1 / 195 (0.51%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 0           |
| Subdural haematoma                              |                 |               |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 1 / 195 (0.51%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 1           |
| Post procedural haemorrhage                     |                 |               |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 0 / 195 (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           |
| Postoperative wound complication                |                 |               |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 0 / 195 (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           |
| Procedural pain                                 |                 |               |                 |

|   |                 |               |                 |
|---|-----------------|---------------|-----------------|
| subjects affected / exposed                     | 2 / 133 (1.50%) | 0 / 8 (0.00%) | 0 / 195 (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           |
| Recall phenomenon                               |                 |               |                 |
| subjects affected / exposed                     | 1 / 133 (0.75%) | 0 / 8 (0.00%) | 0 / 195 (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           |
| Spinal compression fracture                     |                 |               |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 1 / 195 (0.51%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 0           |
| Cardiac disorders                               |                 |               |                 |
| Acute coronary syndrome                         |                 |               |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 0 / 195 (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           |
| Cardiac failure                                 |                 |               |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 0 / 195 (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           |
| Cardiac tamponade                               |                 |               |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 1 / 195 (0.51%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 1           |
| Cardiac arrest                                  |                 |               |                 |
| subjects affected / exposed                     | 2 / 133 (1.50%) | 0 / 8 (0.00%) | 0 / 195 (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           |
| Autoimmune pericarditis                         |                 |               |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 1 / 195 (0.51%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         | 1 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 0           |
| Atrial fibrillation                             |                 |               |                 |

|   |                 |                |                 |
|---|-----------------|----------------|-----------------|
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%)  | 2 / 195 (1.03%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 0 / 2           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0           |
| Coronary artery disease                         |                 |                |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%)  | 1 / 195 (0.51%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0           |
| Acute myocardial infarction                     |                 |                |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%)  | 0 / 195 (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           |
| Angina pectoris                                 |                 |                |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 1 / 8 (12.50%) | 1 / 195 (0.51%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1          | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0           |
| Mitral valve incompetence                       |                 |                |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%)  | 0 / 195 (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           |
| Supraventricular tachycardia                    |                 |                |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%)  | 1 / 195 (0.51%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0           |
| Sinus bradycardia                               |                 |                |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%)  | 1 / 195 (0.51%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0           |
| Pericardial effusion                            |                 |                |                 |
| subjects affected / exposed                     | 2 / 133 (1.50%) | 0 / 8 (0.00%)  | 2 / 195 (1.03%) |
| occurrences causally related to treatment / all | 1 / 2           | 0 / 0          | 0 / 2           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 1           |
| Myocarditis                                     |                 |                |                 |

|   |                 |                |                 |
|---|-----------------|----------------|-----------------|
| subjects affected / exposed                     | 1 / 133 (0.75%) | 0 / 8 (0.00%)  | 1 / 195 (0.51%) |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0          | 1 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0           |
| Myocardial infarction                           |                 |                |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 1 / 8 (12.50%) | 0 / 195 (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           |
| Nervous system disorders                        |                 |                |                 |
| Cerebrovascular accident                        |                 |                |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%)  | 1 / 195 (0.51%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0           |
| Cerebral ischaemia                              |                 |                |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%)  | 1 / 195 (0.51%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0           |
| Cerebral infarction                             |                 |                |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%)  | 0 / 195 (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           |
| Cerebral haemorrhage                            |                 |                |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%)  | 1 / 195 (0.51%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 1           |
| Carotid artery aneurysm                         |                 |                |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%)  | 0 / 195 (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           |
| Bell's palsy                                    |                 |                |                 |
| subjects affected / exposed                     | 1 / 133 (0.75%) | 0 / 8 (0.00%)  | 0 / 195 (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           |
| Basal ganglia infarction                        |                 |                |                 |

|   |                 |               |                 |
|---|-----------------|---------------|-----------------|
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 0 / 195 (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           |
| Headache  |                 |               |                 |
| subjects affected / exposed                     | 1 / 133 (0.75%) | 0 / 8 (0.00%) | 0 / 195 (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           |
| Haemorrhage intracranial                        |                 |               |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 1 / 195 (0.51%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 1           |
| Guillain-Barre syndrome                         |                 |               |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 0 / 195 (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           |
| Encephalopathy                                  |                 |               |                 |
| subjects affected / exposed                     | 1 / 133 (0.75%) | 0 / 8 (0.00%) | 0 / 195 (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           |
| Embolic stroke                                  |                 |               |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 1 / 195 (0.51%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 0           |
| Dizziness                                       |                 |               |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 1 / 195 (0.51%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         | 1 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 0           |
| Depressed level of consciousness                |                 |               |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 1 / 195 (0.51%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 1           |
| Intraventricular haemorrhage                    |                 |               |                 |

|   |                 |               |                 |
|---|-----------------|---------------|-----------------|
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 1 / 195 (0.51%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 1           |
| Syncope   |                 |               |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 3 / 195 (1.54%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         | 0 / 4           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 0           |
| Spinal cord compression                         |                 |               |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 3 / 195 (1.54%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         | 0 / 3           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 0           |
| Seizure   |                 |               |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 0 / 195 (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           |
| Peripheral sensory neuropathy                   |                 |               |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 1 / 195 (0.51%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         | 2 / 2           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 0           |
| Peripheral motor neuropathy                     |                 |               |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 0 / 195 (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           |
| Myasthenia gravis                               |                 |               |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 0 / 195 (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           |
| Monoparesis                                     |                 |               |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 0 / 195 (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           |
| Blood and lymphatic system disorders            |                 |               |                 |
| Febrile neutropenia                             |                 |               |                 |



|   |                 |               |                 |
|---|-----------------|---------------|-----------------|
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 1 / 195 (0.51%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 0           |
| Anaemia   |                 |               |                 |
| subjects affected / exposed                     | 5 / 133 (3.76%) | 0 / 8 (0.00%) | 1 / 195 (0.51%) |
| occurrences causally related to treatment / all | 3 / 6           | 0 / 0         | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 0           |
| Lymph node pain                                 |                 |               |                 |
| subjects affected / exposed                     | 1 / 133 (0.75%) | 0 / 8 (0.00%) | 0 / 195 (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           |
| Iron deficiency anaemia                         |                 |               |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 0 / 195 (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                                   |                 |               |                 |
| Uveitis   |                 |               |                 |
| subjects affected / exposed                     | 1 / 133 (0.75%) | 0 / 8 (0.00%) | 0 / 195 (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                     | 1 / 133 (0.75%) | 0 / 8 (0.00%) | 0 / 195 (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           |
| Abdominal pain                                  |                 |               |                 |
| subjects affected / exposed                     | 2 / 133 (1.50%) | 0 / 8 (0.00%) | 3 / 195 (1.54%) |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 0         | 1 / 3           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 0           |
| Constipation                                    |                 |               |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 1 / 195 (0.51%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 0           |
| Colitis   |                 |               |                 |

|   |                  |               |                 |
|---|------------------|---------------|-----------------|
| subjects affected / exposed                     | 11 / 133 (8.27%) | 0 / 8 (0.00%) | 3 / 195 (1.54%) |
| occurrences causally related to treatment / all | 13 / 13          | 0 / 0         | 3 / 3           |
| deaths causally related to treatment / all      | 1 / 1            | 0 / 0         | 0 / 0           |
| Ascites   |                  |               |                 |
| subjects affected / exposed                     | 1 / 133 (0.75%)  | 0 / 8 (0.00%) | 1 / 195 (0.51%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0         | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0         | 0 / 0           |
| Anorectal disorder                              |                  |               |                 |
| subjects affected / exposed                     | 1 / 133 (0.75%)  | 0 / 8 (0.00%) | 0 / 195 (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           |
| Anal fistula                                    |                  |               |                 |
| subjects affected / exposed                     | 1 / 133 (0.75%)  | 0 / 8 (0.00%) | 0 / 195 (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           |
| Abdominal pain lower                            |                  |               |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%)  | 0 / 8 (0.00%) | 0 / 195 (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           |
| Gastritis                                       |                  |               |                 |
| subjects affected / exposed                     | 2 / 133 (1.50%)  | 0 / 8 (0.00%) | 1 / 195 (0.51%) |
| occurrences causally related to treatment / all | 2 / 2            | 0 / 0         | 1 / 1           |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0         | 0 / 0           |
| Dysphagia                                       |                  |               |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%)  | 0 / 8 (0.00%) | 3 / 195 (1.54%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0         | 0 / 3           |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0         | 0 / 0           |
| Diarrhoea                                       |                  |               |                 |
| subjects affected / exposed                     | 4 / 133 (3.01%)  | 0 / 8 (0.00%) | 9 / 195 (4.62%) |
| occurrences causally related to treatment / all | 3 / 4            | 0 / 0         | 8 / 11          |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0         | 0 / 0           |
| Gastrointestinal haemorrhage                    |                  |               |                 |

|   |                 |               |                 |
|---|-----------------|---------------|-----------------|
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 1 / 195 (0.51%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 0           |
| Gastrointestinal motility disorder              |                 |               |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 1 / 195 (0.51%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         | 1 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 1 / 1           |
| Glossodynia                                     |                 |               |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 0 / 195 (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           |
| Ileus   |                 |               |                 |
| subjects affected / exposed                     | 2 / 133 (1.50%) | 0 / 8 (0.00%) | 0 / 195 (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           |
| Immune-mediated enterocolitis                   |                 |               |                 |
| subjects affected / exposed                     | 3 / 133 (2.26%) | 0 / 8 (0.00%) | 1 / 195 (0.51%) |
| occurrences causally related to treatment / all | 3 / 3           | 0 / 0         | 1 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 0           |
| Intestinal perforation                          |                 |               |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 1 / 195 (0.51%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 1           |
| Intestinal obstruction                          |                 |               |                 |
| subjects affected / exposed                     | 7 / 133 (5.26%) | 0 / 8 (0.00%) | 0 / 195 (0.00%) |
| occurrences causally related to treatment / all | 0 / 9           | 0 / 0         | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 0           |
| Immune-mediated pancreatitis                    |                 |               |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 1 / 195 (0.51%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         | 1 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 0           |
| Large intestinal obstruction                    |                 |               |                 |

|   |                 |               |                 |
|---|-----------------|---------------|-----------------|
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 1 / 195 (0.51%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 0           |
| Oesophagitis                                    |                 |               |                 |
| subjects affected / exposed                     | 1 / 133 (0.75%) | 0 / 8 (0.00%) | 0 / 195 (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           |
| Oesophageal motility disorder                   |                 |               |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 0 / 195 (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           |
| Nausea  |                 |               |                 |
| subjects affected / exposed                     | 1 / 133 (0.75%) | 0 / 8 (0.00%) | 2 / 195 (1.03%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0         | 0 / 2           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 0           |
| Mouth haemorrhage                               |                 |               |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 0 / 195 (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                     | 2 / 133 (1.50%) | 0 / 8 (0.00%) | 4 / 195 (2.05%) |
| occurrences causally related to treatment / all | 1 / 2           | 0 / 0         | 2 / 4           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 0           |
| Pancreatitis                                    |                 |               |                 |
| subjects affected / exposed                     | 1 / 133 (0.75%) | 0 / 8 (0.00%) | 0 / 195 (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           |
| Proctalgia                                      |                 |               |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 1 / 195 (0.51%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         | 0 / 2           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 0           |
| Small intestinal obstruction                    |                 |               |                 |

|   |                 |               |                 |
|---|-----------------|---------------|-----------------|
| subjects affected / exposed                     | 1 / 133 (0.75%) | 0 / 8 (0.00%) | 1 / 195 (0.51%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0         | 0 / 2           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 0           |
| Stomatitis                                      |                 |               |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 1 / 195 (0.51%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         | 0 / 2           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 0           |
| Hepatobiliary disorders                         |                 |               |                 |
| Autoimmune cholangitis                          |                 |               |                 |
| subjects affected / exposed                     | 1 / 133 (0.75%) | 0 / 8 (0.00%) | 0 / 195 (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           |
| Cholecystitis                                   |                 |               |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 0 / 195 (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           |
| Biliary tract disorder                          |                 |               |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 0 / 195 (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           |
| Biliary obstruction                             |                 |               |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 1 / 195 (0.51%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 0           |
| Bile duct stenosis                              |                 |               |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 1 / 195 (0.51%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         | 0 / 2           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 0           |
| Autoimmune hepatitis                            |                 |               |                 |
| subjects affected / exposed                     | 3 / 133 (2.26%) | 0 / 8 (0.00%) | 1 / 195 (0.51%) |
| occurrences causally related to treatment / all | 3 / 3           | 0 / 0         | 1 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 0           |
| Gallbladder rupture                             |                 |               |                 |

|   |                 |               |                 |
|---|-----------------|---------------|-----------------|
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 1 / 195 (0.51%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 0           |
| Hypertransaminasaemia                           |                 |               |                 |
| subjects affected / exposed                     | 3 / 133 (2.26%) | 0 / 8 (0.00%) | 0 / 195 (0.00%) |
| occurrences causally related to treatment / all | 3 / 3           | 0 / 0         | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 0           |
| Hepatotoxicity                                  |                 |               |                 |
| subjects affected / exposed                     | 6 / 133 (4.51%) | 0 / 8 (0.00%) | 0 / 195 (0.00%) |
| occurrences causally related to treatment / all | 6 / 6           | 0 / 0         | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 0           |
| Hepatitis toxic                                 |                 |               |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 1 / 195 (0.51%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 1           |
| Hepatitis                                       |                 |               |                 |
| subjects affected / exposed                     | 1 / 133 (0.75%) | 0 / 8 (0.00%) | 0 / 195 (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           |
| Hepatic function abnormal                       |                 |               |                 |
| subjects affected / exposed                     | 1 / 133 (0.75%) | 0 / 8 (0.00%) | 0 / 195 (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           |
| Hepatic cytolysis                               |                 |               |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 0 / 195 (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           |
| Skin and subcutaneous tissue disorders          |                 |               |                 |
| Hyperhidrosis                                   |                 |               |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 0 / 195 (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           |
| Rash  |                 |               |                 |

|   |                 |               |                 |
|---|-----------------|---------------|-----------------|
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 2 / 195 (1.03%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         | 2 / 3           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 1 / 1           |
| Rash maculo-papular                             |                 |               |                 |
| subjects affected / exposed                     | 1 / 133 (0.75%) | 0 / 8 (0.00%) | 0 / 195 (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           |
| Rash pruritic                                   |                 |               |                 |
| subjects affected / exposed                     | 1 / 133 (0.75%) | 0 / 8 (0.00%) | 0 / 195 (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           |
| Renal and urinary disorders                     |                 |               |                 |
| Hydronephrosis                                  |                 |               |                 |
| subjects affected / exposed                     | 2 / 133 (1.50%) | 0 / 8 (0.00%) | 2 / 195 (1.03%) |
| occurrences causally related to treatment / all | 0 / 3           | 0 / 0         | 0 / 2           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 0           |
| Haematuria                                      |                 |               |                 |
| subjects affected / exposed                     | 1 / 133 (0.75%) | 0 / 8 (0.00%) | 0 / 195 (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           |
| Autoimmune nephritis                            |                 |               |                 |
| subjects affected / exposed                     | 1 / 133 (0.75%) | 0 / 8 (0.00%) | 0 / 195 (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           |
| Acute kidney injury                             |                 |               |                 |
| subjects affected / exposed                     | 8 / 133 (6.02%) | 0 / 8 (0.00%) | 5 / 195 (2.56%) |
| occurrences causally related to treatment / all | 4 / 8           | 0 / 0         | 0 / 5           |
| deaths causally related to treatment / all      | 0 / 1           | 0 / 0         | 0 / 0           |
| Oliguria  |                 |               |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 1 / 195 (0.51%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 0           |
| Renal colic                                     |                 |               |                 |

|   |                 |               |                 |
|---|-----------------|---------------|-----------------|
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 0 / 195 (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           |
| Urogenital fistula                              |                 |               |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 1 / 195 (0.51%) |
| 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 obstruction                       |                 |               |                 |
| subjects affected / exposed                     | 1 / 133 (0.75%) | 0 / 8 (0.00%) | 2 / 195 (1.03%) |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 0         | 0 / 2           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 0           |
| Urinary retention                               |                 |               |                 |
| subjects affected / exposed                     | 1 / 133 (0.75%) | 0 / 8 (0.00%) | 0 / 195 (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 incontinence                            |                 |               |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 1 / 195 (0.51%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 0           |
| Ureteric stenosis                               |                 |               |                 |
| subjects affected / exposed                     | 1 / 133 (0.75%) | 0 / 8 (0.00%) | 0 / 195 (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           |
| Renal haematoma                                 |                 |               |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 0 / 195 (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 / 133 (0.00%) | 0 / 8 (0.00%) | 3 / 195 (1.54%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         | 1 / 3           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 0           |
| Endocrine disorders                             |                 |               |                 |
| Adrenal insufficiency                           |                 |               |                 |



|   |                 |               |                 |
|---|-----------------|---------------|-----------------|
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 4 / 195 (2.05%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         | 4 / 4           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 0           |
| Glucocorticoid deficiency                       |                 |               |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 1 / 195 (0.51%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         | 1 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 0           |
| Thyroid disorder                                |                 |               |                 |
| subjects affected / exposed                     | 1 / 133 (0.75%) | 0 / 8 (0.00%) | 0 / 195 (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           |
| Inappropriate antidiuretic hormone secretion    |                 |               |                 |
| subjects affected / exposed                     | 1 / 133 (0.75%) | 0 / 8 (0.00%) | 0 / 195 (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           |
| Hypothyroidism                                  |                 |               |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 1 / 195 (0.51%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         | 1 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 0           |
| Hypophysitis                                    |                 |               |                 |
| subjects affected / exposed                     | 3 / 133 (2.26%) | 0 / 8 (0.00%) | 0 / 195 (0.00%) |
| occurrences causally related to treatment / all | 4 / 4           | 0 / 0         | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 0           |
| Hyperthyroidism                                 |                 |               |                 |
| subjects affected / exposed                     | 1 / 133 (0.75%) | 0 / 8 (0.00%) | 1 / 195 (0.51%) |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0         | 1 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 0           |
| Musculoskeletal and connective tissue disorders |                 |               |                 |
| Pain in extremity                               |                 |               |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 4 / 195 (2.05%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         | 1 / 5           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 0           |
| Myositis  |                 |               |                 |

|   |                 |                |                 |
|---|-----------------|----------------|-----------------|
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%)  | 1 / 195 (0.51%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 1 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0           |
| Muscular weakness                               |                 |                |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%)  | 2 / 195 (1.03%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 1 / 2           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0           |
| Intervertebral disc protrusion                  |                 |                |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%)  | 0 / 195 (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                     | 0 / 133 (0.00%) | 0 / 8 (0.00%)  | 2 / 195 (1.03%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 0 / 2           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0           |
| Fistula   |                 |                |                 |
| subjects affected / exposed                     | 1 / 133 (0.75%) | 0 / 8 (0.00%)  | 0 / 195 (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                     | 1 / 133 (0.75%) | 0 / 8 (0.00%)  | 2 / 195 (1.03%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0          | 0 / 2           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0           |
| Arthralgia                                      |                 |                |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%)  | 2 / 195 (1.03%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 0 / 2           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0           |
| Pathological fracture                           |                 |                |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 1 / 8 (12.50%) | 1 / 195 (0.51%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1          | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0           |
| Infections and infestations                     |                 |                |                 |
| Cellulitis                                      |                 |                |                 |

|   |                 |               |                 |
|---|-----------------|---------------|-----------------|
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 1 / 195 (0.51%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         | 0 / 3           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 0           |
| Catheter site infection                         |                 |               |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 1 / 195 (0.51%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 0           |
| COVID-19  |                 |               |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 1 / 195 (0.51%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 0           |
| Bacteraemia                                     |                 |               |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 0 / 195 (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           |
| Arthritis bacterial                             |                 |               |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 1 / 195 (0.51%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 0           |
| Abscess neck                                    |                 |               |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 0 / 195 (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           |
| Gastroenteritis                                 |                 |               |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 0 / 195 (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           |
| Encephalitis                                    |                 |               |                 |
| subjects affected / exposed                     | 1 / 133 (0.75%) | 0 / 8 (0.00%) | 0 / 195 (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           |
| Device related sepsis                           |                 |               |                 |

|   |                 |               |                 |
|---|-----------------|---------------|-----------------|
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 0 / 195 (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 / 133 (0.00%) | 0 / 8 (0.00%) | 0 / 195 (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           |
| Clostridium difficile colitis                   |                 |               |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 0 / 195 (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           |
| Clostridial sepsis                              |                 |               |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 1 / 195 (0.51%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 0           |
| Gastroenteritis bacterial                       |                 |               |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 0 / 195 (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           |
| Kidney infection                                |                 |               |                 |
| subjects affected / exposed                     | 1 / 133 (0.75%) | 0 / 8 (0.00%) | 0 / 195 (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           |
| Osteomyelitis                                   |                 |               |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 0 / 195 (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           |
| Meningitis aseptic                              |                 |               |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 1 / 195 (0.51%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         | 2 / 2           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 0           |
| Meningitis                                      |                 |               |                 |

|   |                 |               |                 |
|---|-----------------|---------------|-----------------|
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 1 / 195 (0.51%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 0           |
| Medical device site infection                   |                 |               |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 0 / 195 (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           |
| Lower respiratory tract infection               |                 |               |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 3 / 195 (1.54%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         | 0 / 4           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 0           |
| Localised infection                             |                 |               |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 1 / 195 (0.51%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 1           |
| Large intestine infection                       |                 |               |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 0 / 195 (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           |
| Postoperative wound infection                   |                 |               |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 0 / 195 (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           |
| Post procedural infection                       |                 |               |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 0 / 195 (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           |
| Pneumonia bacterial                             |                 |               |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 0 / 195 (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           |
| Pneumonia aspiration                            |                 |               |                 |

|   |                 |               |                 |
|---|-----------------|---------------|-----------------|
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 0 / 195 (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           |
| Pneumonia                                       |                 |               |                 |
| subjects affected / exposed                     | 1 / 133 (0.75%) | 0 / 8 (0.00%) | 3 / 195 (1.54%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0         | 0 / 3           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 0           |
| Periorbital infection                           |                 |               |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 1 / 195 (0.51%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 0           |
| Otitis media                                    |                 |               |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 0 / 195 (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 sepsis                                |                 |               |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 1 / 195 (0.51%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 0           |
| Respiratory tract infection                     |                 |               |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 1 / 195 (0.51%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 0           |
| Sepsis  |                 |               |                 |
| subjects affected / exposed                     | 4 / 133 (3.01%) | 0 / 8 (0.00%) | 6 / 195 (3.08%) |
| occurrences causally related to treatment / all | 0 / 4           | 0 / 0         | 0 / 8           |
| deaths causally related to treatment / all      | 0 / 1           | 0 / 0         | 0 / 1           |
| Septic shock                                    |                 |               |                 |
| subjects affected / exposed                     | 1 / 133 (0.75%) | 0 / 8 (0.00%) | 1 / 195 (0.51%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0         | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 1           | 0 / 0         | 0 / 1           |
| Sinusitis                                       |                 |               |                 |

|   |                 |               |                  |
|---|-----------------|---------------|------------------|
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 1 / 195 (0.51%)  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 0            |
| Skin infection                                  |                 |               |                  |
| subjects affected / exposed                     | 2 / 133 (1.50%) | 0 / 8 (0.00%) | 1 / 195 (0.51%)  |
| occurrences causally related to treatment / all | 1 / 2           | 0 / 0         | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 0            |
| Soft tissue infection                           |                 |               |                  |
| subjects affected / exposed                     | 1 / 133 (0.75%) | 0 / 8 (0.00%) | 0 / 195 (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                                  |                 |               |                  |
| subjects affected / exposed                     | 4 / 133 (3.01%) | 0 / 8 (0.00%) | 1 / 195 (0.51%)  |
| occurrences causally related to treatment / all | 0 / 5           | 0 / 0         | 0 / 1            |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 0            |
| Pyelonephritis acute                            |                 |               |                  |
| subjects affected / exposed                     | 1 / 133 (0.75%) | 0 / 8 (0.00%) | 0 / 195 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 3           | 0 / 0         | 0 / 0            |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 0            |
| Tuberculosis                                    |                 |               |                  |
| subjects affected / exposed                     | 1 / 133 (0.75%) | 0 / 8 (0.00%) | 0 / 195 (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            |
| Upper respiratory tract infection               |                 |               |                  |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 1 / 195 (0.51%)  |
| 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                     | 7 / 133 (5.26%) | 0 / 8 (0.00%) | 11 / 195 (5.64%) |
| occurrences causally related to treatment / all | 0 / 9           | 0 / 0         | 0 / 17           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 0            |
| Urosepsis                                       |                 |               |                  |

|   |                 |               |                 |
|---|-----------------|---------------|-----------------|
| subjects affected / exposed                     | 1 / 133 (0.75%) | 0 / 8 (0.00%) | 1 / 195 (0.51%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0         | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 0           |
| Vascular device infection                       |                 |               |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 2 / 195 (1.03%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         | 0 / 2           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 0           |
| Metabolism and nutrition disorders              |                 |               |                 |
| Decreased appetite                              |                 |               |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 0 / 195 (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           |
| Dehydration                                     |                 |               |                 |
| subjects affected / exposed                     | 2 / 133 (1.50%) | 0 / 8 (0.00%) | 4 / 195 (2.05%) |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 0         | 0 / 4           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 0           |
| Hypercalcaemia                                  |                 |               |                 |
| subjects affected / exposed                     | 1 / 133 (0.75%) | 0 / 8 (0.00%) | 4 / 195 (2.05%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0         | 0 / 4           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 0           |
| Hyperglycaemia                                  |                 |               |                 |
| subjects affected / exposed                     | 1 / 133 (0.75%) | 0 / 8 (0.00%) | 1 / 195 (0.51%) |
| occurrences causally related to treatment / all | 2 / 2           | 0 / 0         | 1 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 0           |
| Hyperkalaemia                                   |                 |               |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 1 / 195 (0.51%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 0           |
| Hypokalaemia                                    |                 |               |                 |
| subjects affected / exposed                     | 1 / 133 (0.75%) | 0 / 8 (0.00%) | 2 / 195 (1.03%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0         | 0 / 2           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 1           |
| Hyponatraemia                                   |                 |               |                 |



|   |                 |               |                 |
|---|-----------------|---------------|-----------------|
| subjects affected / exposed                     | 1 / 133 (0.75%) | 0 / 8 (0.00%) | 2 / 195 (1.03%) |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0         | 0 / 2           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 0           |
| Hypophagia                                      |                 |               |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 0 / 195 (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           |
| Type 1 diabetes mellitus                        |                 |               |                 |
| subjects affected / exposed                     | 0 / 133 (0.00%) | 0 / 8 (0.00%) | 2 / 195 (1.03%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         | 2 / 2           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         | 0 / 0           |
| Diabetic ketoacidosis                           |                 |               |                 |
| subjects affected / exposed                     | 1 / 133 (0.75%) | 0 / 8 (0.00%) | 0 / 195 (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           |

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

| <b>Non-serious adverse events</b>                                   | Metastatic Monotherapy | Neoadjuvant        | Metastatic Combo D |
|---|------------------------|--------------------|--------------------|
| Total subjects affected by non-serious adverse events               |                        |                    |                    |
| subjects affected / exposed   | 110 / 113 (97.35%)     | 108 / 123 (87.80%) | 5 / 6 (83.33%)     |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                        |                    |                    |
| Tumour pain   |                        |                    |                    |
| subjects affected / exposed   | 7 / 113 (6.19%)        | 1 / 123 (0.81%)    | 0 / 6 (0.00%)      |
| occurrences (all)   | 7                      | 1                  | 0                  |
| Squamous cell carcinoma of skin                                     |                        |                    |                    |
| subjects affected / exposed   | 3 / 113 (2.65%)        | 0 / 123 (0.00%)    | 1 / 6 (16.67%)     |
| occurrences (all)   | 3                      | 0                  | 1                  |
| Vascular disorders  |                        |                    |                    |
| Lymphoedema   |                        |                    |                    |
| subjects affected / exposed   | 4 / 113 (3.54%)        | 2 / 123 (1.63%)    | 1 / 6 (16.67%)     |
| occurrences (all)   | 4                      | 2                  | 1                  |
| Hypotension   |                        |                    |                    |

|  |                   |                   |                |
|--|-------------------|-------------------|----------------|
| subjects affected / exposed                          | 5 / 113 (4.42%)   | 4 / 123 (3.25%)   | 1 / 6 (16.67%) |
| occurrences (all)                                    | 5                 | 4                 | 1              |
| Hypertension   |                   |                   |                |
| subjects affected / exposed                          | 10 / 113 (8.85%)  | 12 / 123 (9.76%)  | 0 / 6 (0.00%)  |
| occurrences (all)                                    | 13                | 12                | 0              |
| Haematoma  |                   |                   |                |
| subjects affected / exposed                          | 2 / 113 (1.77%)   | 2 / 123 (1.63%)   | 0 / 6 (0.00%)  |
| occurrences (all)                                    | 2                 | 2                 | 0              |
| Venous thrombosis                                    |                   |                   |                |
| subjects affected / exposed                          | 1 / 113 (0.88%)   | 0 / 123 (0.00%)   | 1 / 6 (16.67%) |
| occurrences (all)                                    | 1                 | 0                 | 1              |
| General disorders and administration site conditions |                   |                   |                |
| Inflammation   |                   |                   |                |
| subjects affected / exposed                          | 1 / 113 (0.88%)   | 0 / 123 (0.00%)   | 1 / 6 (16.67%) |
| occurrences (all)                                    | 1                 | 0                 | 1              |
| Gait disturbance                                     |                   |                   |                |
| subjects affected / exposed                          | 0 / 113 (0.00%)   | 0 / 123 (0.00%)   | 1 / 6 (16.67%) |
| occurrences (all)                                    | 0                 | 0                 | 1              |
| Fatigue  |                   |                   |                |
| subjects affected / exposed                          | 47 / 113 (41.59%) | 40 / 123 (32.52%) | 1 / 6 (16.67%) |
| occurrences (all)                                    | 60                | 43                | 1              |
| Facial pain  |                   |                   |                |
| subjects affected / exposed                          | 3 / 113 (2.65%)   | 3 / 123 (2.44%)   | 1 / 6 (16.67%) |
| occurrences (all)                                    | 3                 | 3                 | 1              |
| Face oedema  |                   |                   |                |
| subjects affected / exposed                          | 2 / 113 (1.77%)   | 3 / 123 (2.44%)   | 1 / 6 (16.67%) |
| occurrences (all)                                    | 2                 | 3                 | 1              |
| Chills   |                   |                   |                |
| subjects affected / exposed                          | 6 / 113 (5.31%)   | 3 / 123 (2.44%)   | 0 / 6 (0.00%)  |
| occurrences (all)                                    | 7                 | 3                 | 0              |
| Chest pain   |                   |                   |                |
| subjects affected / exposed                          | 6 / 113 (5.31%)   | 0 / 123 (0.00%)   | 0 / 6 (0.00%)  |
| occurrences (all)                                    | 6                 | 0                 | 0              |
| Asthenia   |                   |                   |                |

|   |                   |                   |                |
|---|-------------------|-------------------|----------------|
| subjects affected / exposed                     | 18 / 113 (15.93%) | 11 / 123 (8.94%)  | 0 / 6 (0.00%)  |
| occurrences (all)                               | 26                | 11                | 0              |
| Influenza like illness                          |                   |                   |                |
| subjects affected / exposed                     | 4 / 113 (3.54%)   | 3 / 123 (2.44%)   | 0 / 6 (0.00%)  |
| occurrences (all)                               | 4                 | 3                 | 0              |
| Malaise   |                   |                   |                |
| subjects affected / exposed                     | 4 / 113 (3.54%)   | 0 / 123 (0.00%)   | 0 / 6 (0.00%)  |
| occurrences (all)                               | 4                 | 0                 | 0              |
| Localised oedema                                |                   |                   |                |
| subjects affected / exposed                     | 0 / 113 (0.00%)   | 8 / 123 (6.50%)   | 0 / 6 (0.00%)  |
| occurrences (all)                               | 0                 | 8                 | 0              |
| Mucosal inflammation                            |                   |                   |                |
| subjects affected / exposed                     | 4 / 113 (3.54%)   | 15 / 123 (12.20%) | 0 / 6 (0.00%)  |
| occurrences (all)                               | 4                 | 15                | 0              |
| Non-cardiac chest pain                          |                   |                   |                |
| subjects affected / exposed                     | 5 / 113 (4.42%)   | 2 / 123 (1.63%)   | 0 / 6 (0.00%)  |
| occurrences (all)                               | 5                 | 2                 | 0              |
| Pyrexia   |                   |                   |                |
| subjects affected / exposed                     | 14 / 113 (12.39%) | 13 / 123 (10.57%) | 2 / 6 (33.33%) |
| occurrences (all)                               | 17                | 15                | 2              |
| Pain  |                   |                   |                |
| subjects affected / exposed                     | 3 / 113 (2.65%)   | 2 / 123 (1.63%)   | 1 / 6 (16.67%) |
| occurrences (all)                               | 3                 | 2                 | 1              |
| Oedema peripheral                               |                   |                   |                |
| subjects affected / exposed                     | 16 / 113 (14.16%) | 6 / 123 (4.88%)   | 2 / 6 (33.33%) |
| occurrences (all)                               | 16                | 6                 | 2              |
| Reproductive system and breast disorders        |                   |                   |                |
| Vaginal haemorrhage                             |                   |                   |                |
| subjects affected / exposed                     | 1 / 113 (0.88%)   | 4 / 123 (3.25%)   | 0 / 6 (0.00%)  |
| occurrences (all)                               | 3                 | 5                 | 0              |
| Pelvic pain                                     |                   |                   |                |
| subjects affected / exposed                     | 2 / 113 (1.77%)   | 0 / 123 (0.00%)   | 0 / 6 (0.00%)  |
| occurrences (all)                               | 2                 | 0                 | 0              |
| Respiratory, thoracic and mediastinal disorders |                   |                   |                |

|                             |                   |                 |                |
|-----------------------------|-------------------|-----------------|----------------|
| Pneumonitis                 |                   |                 |                |
| subjects affected / exposed | 8 / 113 (7.08%)   | 0 / 123 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)           | 9                 | 0               | 0              |
| Pleural effusion            |                   |                 |                |
| subjects affected / exposed | 4 / 113 (3.54%)   | 0 / 123 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)           | 4                 | 0               | 0              |
| Oropharyngeal pain          |                   |                 |                |
| subjects affected / exposed | 6 / 113 (5.31%)   | 6 / 123 (4.88%) | 1 / 6 (16.67%) |
| occurrences (all)           | 6                 | 8               | 1              |
| Nasal congestion            |                   |                 |                |
| subjects affected / exposed | 5 / 113 (4.42%)   | 1 / 123 (0.81%) | 0 / 6 (0.00%)  |
| occurrences (all)           | 5                 | 1               | 0              |
| Laryngeal inflammation      |                   |                 |                |
| subjects affected / exposed | 0 / 113 (0.00%)   | 1 / 123 (0.81%) | 0 / 6 (0.00%)  |
| occurrences (all)           | 0                 | 1               | 0              |
| Dyspnoea exertional         |                   |                 |                |
| subjects affected / exposed | 7 / 113 (6.19%)   | 1 / 123 (0.81%) | 0 / 6 (0.00%)  |
| occurrences (all)           | 7                 | 1               | 0              |
| Dyspnoea                    |                   |                 |                |
| subjects affected / exposed | 21 / 113 (18.58%) | 3 / 123 (2.44%) | 1 / 6 (16.67%) |
| occurrences (all)           | 25                | 3               | 1              |
| Cough                       |                   |                 |                |
| subjects affected / exposed | 26 / 113 (23.01%) | 7 / 123 (5.69%) | 1 / 6 (16.67%) |
| occurrences (all)           | 33                | 8               | 1              |
| Aspiration                  |                   |                 |                |
| subjects affected / exposed | 0 / 113 (0.00%)   | 3 / 123 (2.44%) | 1 / 6 (16.67%) |
| occurrences (all)           | 0                 | 3               | 1              |
| Productive cough            |                   |                 |                |
| subjects affected / exposed | 3 / 113 (2.65%)   | 3 / 123 (2.44%) | 0 / 6 (0.00%)  |
| occurrences (all)           | 3                 | 3               | 0              |
| Upper-airway cough syndrome |                   |                 |                |
| subjects affected / exposed | 0 / 113 (0.00%)   | 1 / 123 (0.81%) | 0 / 6 (0.00%)  |
| occurrences (all)           | 0                 | 1               | 0              |
| Psychiatric disorders       |                   |                 |                |
| Anxiety                     |                   |                 |                |

|                                      |                   |                 |                |
|--------------------------------------|-------------------|-----------------|----------------|
| subjects affected / exposed          | 10 / 113 (8.85%)  | 9 / 123 (7.32%) | 0 / 6 (0.00%)  |
| occurrences (all)                    | 10                | 9               | 0              |
| Confusional state                    |                   |                 |                |
| subjects affected / exposed          | 1 / 113 (0.88%)   | 0 / 123 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all)                    | 1                 | 0               | 1              |
| Insomnia                             |                   |                 |                |
| subjects affected / exposed          | 10 / 113 (8.85%)  | 2 / 123 (1.63%) | 1 / 6 (16.67%) |
| occurrences (all)                    | 12                | 2               | 1              |
| Investigations                       |                   |                 |                |
| Alanine aminotransferase increased   |                   |                 |                |
| subjects affected / exposed          | 8 / 113 (7.08%)   | 4 / 123 (3.25%) | 0 / 6 (0.00%)  |
| occurrences (all)                    | 10                | 4               | 0              |
| Amylase increased                    |                   |                 |                |
| subjects affected / exposed          | 6 / 113 (5.31%)   | 7 / 123 (5.69%) | 0 / 6 (0.00%)  |
| occurrences (all)                    | 7                 | 7               | 0              |
| Aspartate aminotransferase increased |                   |                 |                |
| subjects affected / exposed          | 10 / 113 (8.85%)  | 1 / 123 (0.81%) | 0 / 6 (0.00%)  |
| occurrences (all)                    | 12                | 2               | 0              |
| Blood alkaline phosphatase increased |                   |                 |                |
| subjects affected / exposed          | 5 / 113 (4.42%)   | 3 / 123 (2.44%) | 0 / 6 (0.00%)  |
| occurrences (all)                    | 5                 | 3               | 0              |
| Blood creatinine increased           |                   |                 |                |
| subjects affected / exposed          | 11 / 113 (9.73%)  | 4 / 123 (3.25%) | 0 / 6 (0.00%)  |
| occurrences (all)                    | 14                | 4               | 0              |
| Breath sounds abnormal               |                   |                 |                |
| subjects affected / exposed          | 0 / 113 (0.00%)   | 1 / 123 (0.81%) | 0 / 6 (0.00%)  |
| occurrences (all)                    | 0                 | 1               | 0              |
| Lipase increased                     |                   |                 |                |
| subjects affected / exposed          | 17 / 113 (15.04%) | 7 / 123 (5.69%) | 0 / 6 (0.00%)  |
| occurrences (all)                    | 30                | 7               | 0              |
| Lymphocyte count decreased           |                   |                 |                |
| subjects affected / exposed          | 1 / 113 (0.88%)   | 2 / 123 (1.63%) | 0 / 6 (0.00%)  |
| occurrences (all)                    | 1                 | 2               | 0              |
| Platelet count decreased             |                   |                 |                |

|  |                        |                         |                     |
|--|------------------------|-------------------------|---------------------|
| subjects affected / exposed<br>occurrences (all)                                     | 0 / 113 (0.00%)<br>0   | 1 / 123 (0.81%)<br>1    | 0 / 6 (0.00%)<br>0  |
| Troponin increased<br>subjects affected / exposed<br>occurrences (all)               | 1 / 113 (0.88%)<br>1   | 0 / 123 (0.00%)<br>0    | 0 / 6 (0.00%)<br>0  |
| Weight decreased<br>subjects affected / exposed<br>occurrences (all)                 | 10 / 113 (8.85%)<br>10 | 15 / 123 (12.20%)<br>15 | 0 / 6 (0.00%)<br>0  |
| White blood cell count decreased<br>subjects affected / exposed<br>occurrences (all) | 2 / 113 (1.77%)<br>3   | 1 / 123 (0.81%)<br>1    | 0 / 6 (0.00%)<br>0  |
| Injury, poisoning and procedural complications                                       |                        |                         |                     |
| Jaw fracture<br>subjects affected / exposed<br>occurrences (all)                     | 0 / 113 (0.00%)<br>0   | 0 / 123 (0.00%)<br>0    | 0 / 6 (0.00%)<br>0  |
| Procedural pain<br>subjects affected / exposed<br>occurrences (all)                  | 3 / 113 (2.65%)<br>3   | 9 / 123 (7.32%)<br>10   | 0 / 6 (0.00%)<br>0  |
| Infusion related reaction<br>subjects affected / exposed<br>occurrences (all)        | 5 / 113 (4.42%)<br>6   | 4 / 123 (3.25%)<br>4    | 0 / 6 (0.00%)<br>0  |
| Fracture<br>subjects affected / exposed<br>occurrences (all)                         | 0 / 113 (0.00%)<br>0   | 0 / 123 (0.00%)<br>0    | 0 / 6 (0.00%)<br>0  |
| Radiation skin injury<br>subjects affected / exposed<br>occurrences (all)            | 1 / 113 (0.88%)<br>1   | 15 / 123 (12.20%)<br>15 | 0 / 6 (0.00%)<br>0  |
| Fall<br>subjects affected / exposed<br>occurrences (all)                             | 0 / 113 (0.00%)<br>0   | 0 / 123 (0.00%)<br>0    | 0 / 6 (0.00%)<br>0  |
| Nervous system disorders   |                        |                         |                     |
| Peripheral sensory neuropathy<br>subjects affected / exposed<br>occurrences (all)    | 2 / 113 (1.77%)<br>2   | 8 / 123 (6.50%)<br>8    | 1 / 6 (16.67%)<br>1 |
| Paraesthesia   |                        |                         |                     |

|   |                         |                         |                     |
|---|-------------------------|-------------------------|---------------------|
| subjects affected / exposed<br>occurrences (all)  | 2 / 113 (1.77%)<br>2    | 3 / 123 (2.44%)<br>3    | 0 / 6 (0.00%)<br>0  |
| Headache<br>subjects affected / exposed<br>occurrences (all)  | 13 / 113 (11.50%)<br>15 | 6 / 123 (4.88%)<br>6    | 2 / 6 (33.33%)<br>2 |
| Dysgeusia<br>subjects affected / exposed<br>occurrences (all)                                       | 7 / 113 (6.19%)<br>7    | 10 / 123 (8.13%)<br>10  | 0 / 6 (0.00%)<br>0  |
| Dizziness<br>subjects affected / exposed<br>occurrences (all)                                       | 12 / 113 (10.62%)<br>12 | 6 / 123 (4.88%)<br>7    | 0 / 6 (0.00%)<br>0  |
| Blood and lymphatic system disorders<br>Anaemia<br>subjects affected / exposed<br>occurrences (all) | 28 / 113 (24.78%)<br>32 | 11 / 123 (8.94%)<br>12  | 2 / 6 (33.33%)<br>4 |
| Ear and labyrinth disorders<br>Ear pain<br>subjects affected / exposed<br>occurrences (all)         | 3 / 113 (2.65%)<br>4    | 2 / 123 (1.63%)<br>2    | 1 / 6 (16.67%)<br>1 |
| Vertigo<br>subjects affected / exposed<br>occurrences (all)   | 6 / 113 (5.31%)<br>9    | 0 / 123 (0.00%)<br>0    | 0 / 6 (0.00%)<br>0  |
| Gastrointestinal disorders<br>Colitis<br>subjects affected / exposed<br>occurrences (all)           | 2 / 113 (1.77%)<br>3    | 4 / 123 (3.25%)<br>5    | 0 / 6 (0.00%)<br>0  |
| Abdominal pain upper<br>subjects affected / exposed<br>occurrences (all)                            | 12 / 113 (10.62%)<br>13 | 1 / 123 (0.81%)<br>1    | 0 / 6 (0.00%)<br>0  |
| Constipation<br>subjects affected / exposed<br>occurrences (all)                                    | 27 / 113 (23.89%)<br>31 | 21 / 123 (17.07%)<br>21 | 0 / 6 (0.00%)<br>0  |
| Abdominal pain<br>subjects affected / exposed<br>occurrences (all)                                  | 18 / 113 (15.93%)<br>20 | 8 / 123 (6.50%)<br>8    | 0 / 6 (0.00%)<br>0  |
| Tongue ulceration   |                         |                         |                     |

|  |                   |                   |                |
|--|-------------------|-------------------|----------------|
| subjects affected / exposed            | 0 / 113 (0.00%)   | 0 / 123 (0.00%)   | 0 / 6 (0.00%)  |
| occurrences (all)                      | 0                 | 0                 | 0              |
| Stomatitis                             |                   |                   |                |
| subjects affected / exposed            | 7 / 113 (6.19%)   | 5 / 123 (4.07%)   | 0 / 6 (0.00%)  |
| occurrences (all)                      | 7                 | 5                 | 0              |
| Nausea                                 |                   |                   |                |
| subjects affected / exposed            | 25 / 113 (22.12%) | 42 / 123 (34.15%) | 3 / 6 (50.00%) |
| occurrences (all)                      | 30                | 47                | 3              |
| Dysphagia                              |                   |                   |                |
| subjects affected / exposed            | 10 / 113 (8.85%)  | 21 / 123 (17.07%) | 0 / 6 (0.00%)  |
| occurrences (all)                      | 10                | 21                | 0              |
| Dyspepsia                              |                   |                   |                |
| subjects affected / exposed            | 4 / 113 (3.54%)   | 0 / 123 (0.00%)   | 0 / 6 (0.00%)  |
| occurrences (all)                      | 4                 | 0                 | 0              |
| Dry mouth                              |                   |                   |                |
| subjects affected / exposed            | 8 / 113 (7.08%)   | 6 / 123 (4.88%)   | 0 / 6 (0.00%)  |
| occurrences (all)                      | 8                 | 6                 | 0              |
| Diarrhoea                              |                   |                   |                |
| subjects affected / exposed            | 31 / 113 (27.43%) | 22 / 123 (17.89%) | 2 / 6 (33.33%) |
| occurrences (all)                      | 54                | 23                | 2              |
| Vomiting                               |                   |                   |                |
| subjects affected / exposed            | 21 / 113 (18.58%) | 14 / 123 (11.38%) | 0 / 6 (0.00%)  |
| occurrences (all)                      | 29                | 17                | 0              |
| Skin and subcutaneous tissue disorders |                   |                   |                |
| Skin ulcer                             |                   |                   |                |
| subjects affected / exposed            | 0 / 113 (0.00%)   | 0 / 123 (0.00%)   | 2 / 6 (33.33%) |
| occurrences (all)                      | 0                 | 0                 | 2              |
| Rash                                   |                   |                   |                |
| subjects affected / exposed            | 17 / 113 (15.04%) | 7 / 123 (5.69%)   | 0 / 6 (0.00%)  |
| occurrences (all)                      | 22                | 7                 | 0              |
| Pruritus                               |                   |                   |                |
| subjects affected / exposed            | 23 / 113 (20.35%) | 11 / 123 (8.94%)  | 1 / 6 (16.67%) |
| occurrences (all)                      | 30                | 11                | 2              |
| Night sweats                           |                   |                   |                |
| subjects affected / exposed            | 1 / 113 (0.88%)   | 1 / 123 (0.81%)   | 0 / 6 (0.00%)  |
| occurrences (all)                      | 1                 | 1                 | 0              |



|   |                         |                        |                     |
|---|-------------------------|------------------------|---------------------|
| Dry skin<br>subjects affected / exposed<br>occurrences (all)            | 10 / 113 (8.85%)<br>10  | 3 / 123 (2.44%)<br>3   | 1 / 6 (16.67%)<br>1 |
| Rash maculo-papular<br>subjects affected / exposed<br>occurrences (all) | 8 / 113 (7.08%)<br>12   | 6 / 123 (4.88%)<br>6   | 0 / 6 (0.00%)<br>0  |
| Endocrine disorders   |                         |                        |                     |
| Hyperthyroidism<br>subjects affected / exposed<br>occurrences (all)     | 2 / 113 (1.77%)<br>2    | 4 / 123 (3.25%)<br>4   | 0 / 6 (0.00%)<br>0  |
| Hypothyroidism<br>subjects affected / exposed<br>occurrences (all)      | 17 / 113 (15.04%)<br>17 | 3 / 123 (2.44%)<br>3   | 1 / 6 (16.67%)<br>1 |
| Musculoskeletal and connective tissue disorders                         |                         |                        |                     |
| Groin pain<br>subjects affected / exposed<br>occurrences (all)          | 2 / 113 (1.77%)<br>2    | 0 / 123 (0.00%)<br>0   | 0 / 6 (0.00%)<br>0  |
| Flank pain<br>subjects affected / exposed<br>occurrences (all)          | 6 / 113 (5.31%)<br>6    | 0 / 123 (0.00%)<br>0   | 0 / 6 (0.00%)<br>0  |
| Back pain<br>subjects affected / exposed<br>occurrences (all)           | 17 / 113 (15.04%)<br>20 | 4 / 123 (3.25%)<br>4   | 1 / 6 (16.67%)<br>1 |
| Arthralgia<br>subjects affected / exposed<br>occurrences (all)          | 24 / 113 (21.24%)<br>28 | 10 / 123 (8.13%)<br>10 | 1 / 6 (16.67%)<br>1 |
| Muscular weakness<br>subjects affected / exposed<br>occurrences (all)   | 2 / 113 (1.77%)<br>2    | 4 / 123 (3.25%)<br>4   | 0 / 6 (0.00%)<br>0  |
| Pain in extremity<br>subjects affected / exposed<br>occurrences (all)   | 12 / 113 (10.62%)<br>12 | 4 / 123 (3.25%)<br>4   | 0 / 6 (0.00%)<br>0  |
| Neck pain<br>subjects affected / exposed<br>occurrences (all)           | 3 / 113 (2.65%)<br>4    | 6 / 123 (4.88%)<br>6   | 0 / 6 (0.00%)<br>0  |
| Myalgia   |                         |                        |                     |

|                             |                  |                 |                |
|-----------------------------|------------------|-----------------|----------------|
| subjects affected / exposed | 10 / 113 (8.85%) | 6 / 123 (4.88%) | 0 / 6 (0.00%)  |
| occurrences (all)           | 10               | 6               | 0              |
| Musculoskeletal pain        |                  |                 |                |
| subjects affected / exposed | 4 / 113 (3.54%)  | 0 / 123 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)           | 4                | 0               | 0              |
| Musculoskeletal chest pain  |                  |                 |                |
| subjects affected / exposed | 8 / 113 (7.08%)  | 0 / 123 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)           | 8                | 0               | 0              |
| Infections and infestations |                  |                 |                |
| Oral bacterial infection    |                  |                 |                |
| subjects affected / exposed | 0 / 113 (0.00%)  | 0 / 123 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)           | 0                | 0               | 0              |
| Nasopharyngitis             |                  |                 |                |
| subjects affected / exposed | 10 / 113 (8.85%) | 0 / 123 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)           | 16               | 0               | 0              |
| Mucosal infection           |                  |                 |                |
| subjects affected / exposed | 2 / 113 (1.77%)  | 1 / 123 (0.81%) | 1 / 6 (16.67%) |
| occurrences (all)           | 2                | 1               | 1              |
| Eye infection               |                  |                 |                |
| subjects affected / exposed | 0 / 113 (0.00%)  | 0 / 123 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all)           | 0                | 0               | 1              |
| Conjunctivitis              |                  |                 |                |
| subjects affected / exposed | 6 / 113 (5.31%)  | 0 / 123 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)           | 7                | 0               | 0              |
| Candida infection           |                  |                 |                |
| subjects affected / exposed | 3 / 113 (2.65%)  | 3 / 123 (2.44%) | 0 / 6 (0.00%)  |
| occurrences (all)           | 3                | 3               | 0              |
| Bronchitis                  |                  |                 |                |
| subjects affected / exposed | 8 / 113 (7.08%)  | 1 / 123 (0.81%) | 0 / 6 (0.00%)  |
| occurrences (all)           | 8                | 1               | 0              |
| Otitis externa              |                  |                 |                |
| subjects affected / exposed | 0 / 113 (0.00%)  | 0 / 123 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)           | 0                | 0               | 0              |
| Urinary tract infection     |                  |                 |                |
| subjects affected / exposed | 9 / 113 (7.96%)  | 9 / 123 (7.32%) | 0 / 6 (0.00%)  |
| occurrences (all)           | 9                | 11              | 0              |

|   |                         |                         |                     |
|---|-------------------------|-------------------------|---------------------|
| Upper respiratory tract infection<br>subjects affected / exposed<br>occurrences (all) | 7 / 113 (6.19%)<br>9    | 0 / 123 (0.00%)<br>0    | 0 / 6 (0.00%)<br>0  |
| Tracheitis<br>subjects affected / exposed<br>occurrences (all)                        | 0 / 113 (0.00%)<br>0    | 0 / 123 (0.00%)<br>0    | 1 / 6 (16.67%)<br>1 |
| Rhinitis<br>subjects affected / exposed<br>occurrences (all)                          | 6 / 113 (5.31%)<br>6    | 0 / 123 (0.00%)<br>0    | 0 / 6 (0.00%)<br>0  |
| Respiratory tract infection<br>subjects affected / exposed<br>occurrences (all)       | 3 / 113 (2.65%)<br>5    | 0 / 123 (0.00%)<br>0    | 1 / 6 (16.67%)<br>1 |
| Metabolism and nutrition disorders  |                         |                         |                     |
| Decreased appetite<br>subjects affected / exposed<br>occurrences (all)                | 24 / 113 (21.24%)<br>29 | 15 / 123 (12.20%)<br>16 | 1 / 6 (16.67%)<br>1 |
| Hypophosphataemia<br>subjects affected / exposed<br>occurrences (all)                 | 5 / 113 (4.42%)<br>8    | 4 / 123 (3.25%)<br>4    | 0 / 6 (0.00%)<br>0  |
| Hyponatraemia<br>subjects affected / exposed<br>occurrences (all)                     | 4 / 113 (3.54%)<br>4    | 9 / 123 (7.32%)<br>9    | 1 / 6 (16.67%)<br>1 |
| Hypokalaemia<br>subjects affected / exposed<br>occurrences (all)                      | 6 / 113 (5.31%)<br>10   | 11 / 123 (8.94%)<br>12  | 0 / 6 (0.00%)<br>0  |
| Hypoalbuminaemia<br>subjects affected / exposed<br>occurrences (all)                  | 2 / 113 (1.77%)<br>2    | 2 / 123 (1.63%)<br>2    | 0 / 6 (0.00%)<br>0  |
| Hyperglycaemia<br>subjects affected / exposed<br>occurrences (all)                    | 3 / 113 (2.65%)<br>3    | 3 / 123 (2.44%)<br>3    | 0 / 6 (0.00%)<br>0  |
| Hypercalcaemia<br>subjects affected / exposed<br>occurrences (all)                    | 3 / 113 (2.65%)<br>5    | 2 / 123 (1.63%)<br>3    | 1 / 6 (16.67%)<br>1 |
| Dehydration   |                         |                         |                     |

|                             |                  |                  |               |
|-----------------------------|------------------|------------------|---------------|
| subjects affected / exposed | 1 / 113 (0.88%)  | 8 / 123 (6.50%)  | 0 / 6 (0.00%) |
| occurrences (all)           | 1                | 9                | 0             |
| Hypomagnesaemia             |                  |                  |               |
| subjects affected / exposed | 10 / 113 (8.85%) | 10 / 123 (8.13%) | 0 / 6 (0.00%) |
| occurrences (all)           | 10               | 10               | 0             |

| <b>Non-serious adverse events</b>                                   | Metastatic Combo B | Metastatic Combo C | Metastatic Combo A |
|---|--------------------|--------------------|--------------------|
| Total subjects affected by non-serious adverse events               |                    |                    |                    |
| subjects affected / exposed   | 129 / 133 (96.99%) | 7 / 8 (87.50%)     | 189 / 195 (96.92%) |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                    |                    |                    |
| Tumour pain   |                    |                    |                    |
| subjects affected / exposed   | 3 / 133 (2.26%)    | 1 / 8 (12.50%)     | 5 / 195 (2.56%)    |
| occurrences (all)   | 3                  | 1                  | 5                  |
| Squamous cell carcinoma of skin                                     |                    |                    |                    |
| subjects affected / exposed   | 0 / 133 (0.00%)    | 0 / 8 (0.00%)      | 1 / 195 (0.51%)    |
| occurrences (all)   | 0                  | 0                  | 1                  |
| Vascular disorders  |                    |                    |                    |
| Lymphoedema   |                    |                    |                    |
| subjects affected / exposed   | 5 / 133 (3.76%)    | 1 / 8 (12.50%)     | 4 / 195 (2.05%)    |
| occurrences (all)   | 5                  | 1                  | 4                  |
| Hypotension   |                    |                    |                    |
| subjects affected / exposed   | 4 / 133 (3.01%)    | 0 / 8 (0.00%)      | 10 / 195 (5.13%)   |
| occurrences (all)   | 5                  | 0                  | 16                 |
| Hypertension  |                    |                    |                    |
| subjects affected / exposed   | 5 / 133 (3.76%)    | 1 / 8 (12.50%)     | 7 / 195 (3.59%)    |
| occurrences (all)   | 5                  | 1                  | 7                  |
| Haematoma   |                    |                    |                    |
| subjects affected / exposed   | 0 / 133 (0.00%)    | 1 / 8 (12.50%)     | 2 / 195 (1.03%)    |
| occurrences (all)   | 0                  | 1                  | 2                  |
| Venous thrombosis   |                    |                    |                    |
| subjects affected / exposed   | 0 / 133 (0.00%)    | 0 / 8 (0.00%)      | 0 / 195 (0.00%)    |
| occurrences (all)   | 0                  | 0                  | 0                  |
| General disorders and administration site conditions                |                    |                    |                    |
| Inflammation  |                    |                    |                    |
| subjects affected / exposed   | 0 / 133 (0.00%)    | 0 / 8 (0.00%)      | 0 / 195 (0.00%)    |
| occurrences (all)   | 0                  | 0                  | 0                  |

|                             |                   |                |                   |
|-----------------------------|-------------------|----------------|-------------------|
| Gait disturbance            |                   |                |                   |
| subjects affected / exposed | 1 / 133 (0.75%)   | 0 / 8 (0.00%)  | 2 / 195 (1.03%)   |
| occurrences (all)           | 1                 | 0              | 2                 |
| Fatigue                     |                   |                |                   |
| subjects affected / exposed | 46 / 133 (34.59%) | 6 / 8 (75.00%) | 81 / 195 (41.54%) |
| occurrences (all)           | 53                | 6              | 85                |
| Facial pain                 |                   |                |                   |
| subjects affected / exposed | 0 / 133 (0.00%)   | 0 / 8 (0.00%)  | 0 / 195 (0.00%)   |
| occurrences (all)           | 0                 | 0              | 0                 |
| Face oedema                 |                   |                |                   |
| subjects affected / exposed | 1 / 133 (0.75%)   | 0 / 8 (0.00%)  | 6 / 195 (3.08%)   |
| occurrences (all)           | 1                 | 0              | 7                 |
| Chills                      |                   |                |                   |
| subjects affected / exposed | 9 / 133 (6.77%)   | 0 / 8 (0.00%)  | 10 / 195 (5.13%)  |
| occurrences (all)           | 11                | 0              | 11                |
| Chest pain                  |                   |                |                   |
| subjects affected / exposed | 1 / 133 (0.75%)   | 1 / 8 (12.50%) | 2 / 195 (1.03%)   |
| occurrences (all)           | 1                 | 1              | 2                 |
| Asthenia                    |                   |                |                   |
| subjects affected / exposed | 23 / 133 (17.29%) | 0 / 8 (0.00%)  | 26 / 195 (13.33%) |
| occurrences (all)           | 25                | 0              | 32                |
| Influenza like illness      |                   |                |                   |
| subjects affected / exposed | 2 / 133 (1.50%)   | 0 / 8 (0.00%)  | 12 / 195 (6.15%)  |
| occurrences (all)           | 2                 | 0              | 14                |
| Malaise                     |                   |                |                   |
| subjects affected / exposed | 0 / 133 (0.00%)   | 1 / 8 (12.50%) | 3 / 195 (1.54%)   |
| occurrences (all)           | 0                 | 1              | 3                 |
| Localised oedema            |                   |                |                   |
| subjects affected / exposed | 0 / 133 (0.00%)   | 0 / 8 (0.00%)  | 2 / 195 (1.03%)   |
| occurrences (all)           | 0                 | 0              | 2                 |
| Mucosal inflammation        |                   |                |                   |
| subjects affected / exposed | 5 / 133 (3.76%)   | 0 / 8 (0.00%)  | 6 / 195 (3.08%)   |
| occurrences (all)           | 8                 | 0              | 6                 |
| Non-cardiac chest pain      |                   |                |                   |
| subjects affected / exposed | 3 / 133 (2.26%)   | 1 / 8 (12.50%) | 3 / 195 (1.54%)   |
| occurrences (all)           | 4                 | 1              | 4                 |

|   |                   |                |                   |
|---|-------------------|----------------|-------------------|
| Pyrexia   |                   |                |                   |
| subjects affected / exposed                     | 33 / 133 (24.81%) | 0 / 8 (0.00%)  | 34 / 195 (17.44%) |
| occurrences (all)                               | 43                | 0              | 37                |
| Pain  |                   |                |                   |
| subjects affected / exposed                     | 4 / 133 (3.01%)   | 1 / 8 (12.50%) | 9 / 195 (4.62%)   |
| occurrences (all)                               | 4                 | 1              | 9                 |
| Oedema peripheral                               |                   |                |                   |
| subjects affected / exposed                     | 20 / 133 (15.04%) | 1 / 8 (12.50%) | 21 / 195 (10.77%) |
| occurrences (all)                               | 22                | 1              | 24                |
| Reproductive system and breast disorders        |                   |                |                   |
| Vaginal haemorrhage                             |                   |                |                   |
| subjects affected / exposed                     | 7 / 133 (5.26%)   | 0 / 8 (0.00%)  | 6 / 195 (3.08%)   |
| occurrences (all)                               | 10                | 0              | 9                 |
| Pelvic pain                                     |                   |                |                   |
| subjects affected / exposed                     | 7 / 133 (5.26%)   | 0 / 8 (0.00%)  | 6 / 195 (3.08%)   |
| occurrences (all)                               | 7                 | 0              | 7                 |
| Respiratory, thoracic and mediastinal disorders |                   |                |                   |
| Pneumonitis                                     |                   |                |                   |
| subjects affected / exposed                     | 9 / 133 (6.77%)   | 0 / 8 (0.00%)  | 9 / 195 (4.62%)   |
| occurrences (all)                               | 10                | 0              | 12                |
| Pleural effusion                                |                   |                |                   |
| subjects affected / exposed                     | 1 / 133 (0.75%)   | 1 / 8 (12.50%) | 4 / 195 (2.05%)   |
| occurrences (all)                               | 1                 | 2              | 5                 |
| Oropharyngeal pain                              |                   |                |                   |
| subjects affected / exposed                     | 3 / 133 (2.26%)   | 0 / 8 (0.00%)  | 10 / 195 (5.13%)  |
| occurrences (all)                               | 4                 | 0              | 11                |
| Nasal congestion                                |                   |                |                   |
| subjects affected / exposed                     | 4 / 133 (3.01%)   | 0 / 8 (0.00%)  | 11 / 195 (5.64%)  |
| occurrences (all)                               | 4                 | 0              | 13                |
| Laryngeal inflammation                          |                   |                |                   |
| subjects affected / exposed                     | 0 / 133 (0.00%)   | 1 / 8 (12.50%) | 0 / 195 (0.00%)   |
| occurrences (all)                               | 0                 | 1              | 0                 |
| Dyspnoea exertional                             |                   |                |                   |
| subjects affected / exposed                     | 1 / 133 (0.75%)   | 0 / 8 (0.00%)  | 4 / 195 (2.05%)   |
| occurrences (all)                               | 1                 | 0              | 4                 |
| Dyspnoea  |                   |                |                   |

|  |                         |                     |                         |
|--|-------------------------|---------------------|-------------------------|
| subjects affected / exposed<br>occurrences (all)   | 13 / 133 (9.77%)<br>16  | 2 / 8 (25.00%)<br>2 | 30 / 195 (15.38%)<br>34 |
| Cough<br>subjects affected / exposed<br>occurrences (all)  | 17 / 133 (12.78%)<br>21 | 2 / 8 (25.00%)<br>3 | 49 / 195 (25.13%)<br>64 |
| Aspiration<br>subjects affected / exposed<br>occurrences (all)   | 0 / 133 (0.00%)<br>0    | 0 / 8 (0.00%)<br>0  | 4 / 195 (2.05%)<br>4    |
| Productive cough<br>subjects affected / exposed<br>occurrences (all)                                     | 7 / 133 (5.26%)<br>8    | 0 / 8 (0.00%)<br>0  | 7 / 195 (3.59%)<br>8    |
| Upper-airway cough syndrome<br>subjects affected / exposed<br>occurrences (all)                          | 1 / 133 (0.75%)<br>1    | 1 / 8 (12.50%)<br>1 | 6 / 195 (3.08%)<br>9    |
| Psychiatric disorders<br>Anxiety<br>subjects affected / exposed<br>occurrences (all)                     | 4 / 133 (3.01%)<br>4    | 1 / 8 (12.50%)<br>1 | 8 / 195 (4.10%)<br>9    |
| Confusional state<br>subjects affected / exposed<br>occurrences (all)                                    | 2 / 133 (1.50%)<br>2    | 0 / 8 (0.00%)<br>0  | 5 / 195 (2.56%)<br>5    |
| Insomnia<br>subjects affected / exposed<br>occurrences (all)   | 8 / 133 (6.02%)<br>8    | 1 / 8 (12.50%)<br>1 | 23 / 195 (11.79%)<br>26 |
| Investigations<br>Alanine aminotransferase increased<br>subjects affected / exposed<br>occurrences (all) | 22 / 133 (16.54%)<br>30 | 0 / 8 (0.00%)<br>0  | 26 / 195 (13.33%)<br>31 |
| Amylase increased<br>subjects affected / exposed<br>occurrences (all)                                    | 12 / 133 (9.02%)<br>14  | 1 / 8 (12.50%)<br>1 | 20 / 195 (10.26%)<br>33 |
| Aspartate aminotransferase increased<br>subjects affected / exposed<br>occurrences (all)                 | 20 / 133 (15.04%)<br>31 | 0 / 8 (0.00%)<br>0  | 25 / 195 (12.82%)<br>31 |
| Blood alkaline phosphatase increased   |                         |                     |                         |

|  |                   |                |                   |
|--|-------------------|----------------|-------------------|
| subjects affected / exposed                    | 7 / 133 (5.26%)   | 0 / 8 (0.00%)  | 10 / 195 (5.13%)  |
| occurrences (all)                              | 8                 | 0              | 15                |
| Blood creatinine increased                     |                   |                |                   |
| subjects affected / exposed                    | 13 / 133 (9.77%)  | 0 / 8 (0.00%)  | 19 / 195 (9.74%)  |
| occurrences (all)                              | 18                | 0              | 32                |
| Breath sounds abnormal                         |                   |                |                   |
| subjects affected / exposed                    | 0 / 133 (0.00%)   | 1 / 8 (12.50%) | 0 / 195 (0.00%)   |
| occurrences (all)                              | 0                 | 2              | 0                 |
| Lipase increased                               |                   |                |                   |
| subjects affected / exposed                    | 17 / 133 (12.78%) | 2 / 8 (25.00%) | 27 / 195 (13.85%) |
| occurrences (all)                              | 18                | 2              | 71                |
| Lymphocyte count decreased                     |                   |                |                   |
| subjects affected / exposed                    | 3 / 133 (2.26%)   | 0 / 8 (0.00%)  | 16 / 195 (8.21%)  |
| occurrences (all)                              | 3                 | 0              | 20                |
| Platelet count decreased                       |                   |                |                   |
| subjects affected / exposed                    | 0 / 133 (0.00%)   | 0 / 8 (0.00%)  | 11 / 195 (5.64%)  |
| occurrences (all)                              | 0                 | 0              | 18                |
| Troponin increased                             |                   |                |                   |
| subjects affected / exposed                    | 0 / 133 (0.00%)   | 1 / 8 (12.50%) | 0 / 195 (0.00%)   |
| occurrences (all)                              | 0                 | 1              | 0                 |
| Weight decreased                               |                   |                |                   |
| subjects affected / exposed                    | 8 / 133 (6.02%)   | 2 / 8 (25.00%) | 24 / 195 (12.31%) |
| occurrences (all)                              | 8                 | 2              | 28                |
| White blood cell count decreased               |                   |                |                   |
| subjects affected / exposed                    | 4 / 133 (3.01%)   | 0 / 8 (0.00%)  | 10 / 195 (5.13%)  |
| occurrences (all)                              | 5                 | 0              | 12                |
| Injury, poisoning and procedural complications |                   |                |                   |
| Jaw fracture                                   |                   |                |                   |
| subjects affected / exposed                    | 0 / 133 (0.00%)   | 1 / 8 (12.50%) | 0 / 195 (0.00%)   |
| occurrences (all)                              | 0                 | 1              | 0                 |
| Procedural pain                                |                   |                |                   |
| subjects affected / exposed                    | 0 / 133 (0.00%)   | 0 / 8 (0.00%)  | 3 / 195 (1.54%)   |
| occurrences (all)                              | 0                 | 0              | 3                 |
| Infusion related reaction                      |                   |                |                   |



|   |                         |                     |                         |
|---|-------------------------|---------------------|-------------------------|
| subjects affected / exposed<br>occurrences (all)  | 4 / 133 (3.01%)<br>5    | 0 / 8 (0.00%)<br>0  | 11 / 195 (5.64%)<br>16  |
| Fracture<br>subjects affected / exposed<br>occurrences (all)  | 0 / 133 (0.00%)<br>0    | 1 / 8 (12.50%)<br>1 | 0 / 195 (0.00%)<br>0    |
| Radiation skin injury<br>subjects affected / exposed<br>occurrences (all)                                     | 0 / 133 (0.00%)<br>0    | 0 / 8 (0.00%)<br>0  | 1 / 195 (0.51%)<br>1    |
| Fall<br>subjects affected / exposed<br>occurrences (all)  | 2 / 133 (1.50%)<br>2    | 1 / 8 (12.50%)<br>1 | 1 / 195 (0.51%)<br>1    |
| Nervous system disorders<br>Peripheral sensory neuropathy<br>subjects affected / exposed<br>occurrences (all) | 4 / 133 (3.01%)<br>4    | 0 / 8 (0.00%)<br>0  | 4 / 195 (2.05%)<br>6    |
| Paraesthesia<br>subjects affected / exposed<br>occurrences (all)  | 2 / 133 (1.50%)<br>2    | 2 / 8 (25.00%)<br>2 | 3 / 195 (1.54%)<br>3    |
| Headache<br>subjects affected / exposed<br>occurrences (all)  | 22 / 133 (16.54%)<br>32 | 0 / 8 (0.00%)<br>0  | 31 / 195 (15.90%)<br>41 |
| Dysgeusia<br>subjects affected / exposed<br>occurrences (all)   | 3 / 133 (2.26%)<br>3    | 0 / 8 (0.00%)<br>0  | 3 / 195 (1.54%)<br>3    |
| Dizziness<br>subjects affected / exposed<br>occurrences (all)   | 15 / 133 (11.28%)<br>19 | 0 / 8 (0.00%)<br>0  | 19 / 195 (9.74%)<br>22  |
| Blood and lymphatic system disorders<br>Anaemia<br>subjects affected / exposed<br>occurrences (all)           | 42 / 133 (31.58%)<br>64 | 2 / 8 (25.00%)<br>3 | 53 / 195 (27.18%)<br>78 |
| Ear and labyrinth disorders<br>Ear pain<br>subjects affected / exposed<br>occurrences (all)                   | 1 / 133 (0.75%)<br>1    | 0 / 8 (0.00%)<br>0  | 4 / 195 (2.05%)<br>4    |
| Vertigo   |                         |                     |                         |

|  |                      |                    |                      |
|--|----------------------|--------------------|----------------------|
| subjects affected / exposed<br>occurrences (all) | 1 / 133 (0.75%)<br>1 | 0 / 8 (0.00%)<br>0 | 1 / 195 (0.51%)<br>2 |
| Gastrointestinal disorders                       |                      |                    |                      |
| Colitis  |                      |                    |                      |
| subjects affected / exposed                      | 7 / 133 (5.26%)      | 0 / 8 (0.00%)      | 6 / 195 (3.08%)      |
| occurrences (all)                                | 8                    | 0                  | 7                    |
| Abdominal pain upper                             |                      |                    |                      |
| subjects affected / exposed                      | 5 / 133 (3.76%)      | 0 / 8 (0.00%)      | 9 / 195 (4.62%)      |
| occurrences (all)                                | 5                    | 0                  | 9                    |
| Constipation                                     |                      |                    |                      |
| subjects affected / exposed                      | 37 / 133 (27.82%)    | 1 / 8 (12.50%)     | 51 / 195 (26.15%)    |
| occurrences (all)                                | 49                   | 1                  | 62                   |
| Abdominal pain                                   |                      |                    |                      |
| subjects affected / exposed                      | 30 / 133 (22.56%)    | 1 / 8 (12.50%)     | 28 / 195 (14.36%)    |
| occurrences (all)                                | 35                   | 1                  | 34                   |
| Tongue ulceration                                |                      |                    |                      |
| subjects affected / exposed                      | 1 / 133 (0.75%)      | 1 / 8 (12.50%)     | 1 / 195 (0.51%)      |
| occurrences (all)                                | 1                    | 1                  | 1                    |
| Stomatitis                                       |                      |                    |                      |
| subjects affected / exposed                      | 4 / 133 (3.01%)      | 0 / 8 (0.00%)      | 5 / 195 (2.56%)      |
| occurrences (all)                                | 4                    | 0                  | 8                    |
| Nausea   |                      |                    |                      |
| subjects affected / exposed                      | 48 / 133 (36.09%)    | 2 / 8 (25.00%)     | 45 / 195 (23.08%)    |
| occurrences (all)                                | 75                   | 2                  | 55                   |
| Dysphagia  |                      |                    |                      |
| subjects affected / exposed                      | 2 / 133 (1.50%)      | 4 / 8 (50.00%)     | 12 / 195 (6.15%)     |
| occurrences (all)                                | 2                    | 4                  | 12                   |
| Dyspepsia  |                      |                    |                      |
| subjects affected / exposed                      | 7 / 133 (5.26%)      | 0 / 8 (0.00%)      | 11 / 195 (5.64%)     |
| occurrences (all)                                | 7                    | 0                  | 12                   |
| Dry mouth  |                      |                    |                      |
| subjects affected / exposed                      | 6 / 133 (4.51%)      | 1 / 8 (12.50%)     | 13 / 195 (6.67%)     |
| occurrences (all)                                | 6                    | 1                  | 15                   |
| Diarrhoea  |                      |                    |                      |
| subjects affected / exposed                      | 54 / 133 (40.60%)    | 1 / 8 (12.50%)     | 61 / 195 (31.28%)    |
| occurrences (all)                                | 91                   | 4                  | 108                  |

|   |                         |                     |                         |
|---|-------------------------|---------------------|-------------------------|
| Vomiting<br>subjects affected / exposed<br>occurrences (all)            | 33 / 133 (24.81%)<br>49 | 1 / 8 (12.50%)<br>1 | 31 / 195 (15.90%)<br>38 |
| Skin and subcutaneous tissue disorders                                  |                         |                     |                         |
| Skin ulcer<br>subjects affected / exposed<br>occurrences (all)          | 1 / 133 (0.75%)<br>1    | 0 / 8 (0.00%)<br>0  | 2 / 195 (1.03%)<br>2    |
| Rash<br>subjects affected / exposed<br>occurrences (all)                | 16 / 133 (12.03%)<br>24 | 1 / 8 (12.50%)<br>1 | 49 / 195 (25.13%)<br>65 |
| Pruritus<br>subjects affected / exposed<br>occurrences (all)            | 35 / 133 (26.32%)<br>40 | 0 / 8 (0.00%)<br>0  | 60 / 195 (30.77%)<br>77 |
| Night sweats<br>subjects affected / exposed<br>occurrences (all)        | 1 / 133 (0.75%)<br>1    | 1 / 8 (12.50%)<br>1 | 3 / 195 (1.54%)<br>3    |
| Dry skin<br>subjects affected / exposed<br>occurrences (all)            | 12 / 133 (9.02%)<br>15  | 0 / 8 (0.00%)<br>0  | 14 / 195 (7.18%)<br>14  |
| Rash maculo-papular<br>subjects affected / exposed<br>occurrences (all) | 25 / 133 (18.80%)<br>29 | 0 / 8 (0.00%)<br>0  | 20 / 195 (10.26%)<br>25 |
| Endocrine disorders   |                         |                     |                         |
| Hyperthyroidism<br>subjects affected / exposed<br>occurrences (all)     | 21 / 133 (15.79%)<br>24 | 0 / 8 (0.00%)<br>0  | 9 / 195 (4.62%)<br>9    |
| Hypothyroidism<br>subjects affected / exposed<br>occurrences (all)      | 31 / 133 (23.31%)<br>31 | 2 / 8 (25.00%)<br>2 | 39 / 195 (20.00%)<br>39 |
| Musculoskeletal and connective tissue disorders                         |                         |                     |                         |
| Groin pain<br>subjects affected / exposed<br>occurrences (all)          | 2 / 133 (1.50%)<br>2    | 1 / 8 (12.50%)<br>1 | 3 / 195 (1.54%)<br>3    |
| Flank pain<br>subjects affected / exposed<br>occurrences (all)          | 7 / 133 (5.26%)<br>8    | 0 / 8 (0.00%)<br>0  | 7 / 195 (3.59%)<br>7    |

|                             |                   |                |                   |
|-----------------------------|-------------------|----------------|-------------------|
| Back pain                   |                   |                |                   |
| subjects affected / exposed | 19 / 133 (14.29%) | 1 / 8 (12.50%) | 28 / 195 (14.36%) |
| occurrences (all)           | 20                | 1              | 34                |
| Arthralgia                  |                   |                |                   |
| subjects affected / exposed | 26 / 133 (19.55%) | 2 / 8 (25.00%) | 35 / 195 (17.95%) |
| occurrences (all)           | 29                | 2              | 44                |
| Muscular weakness           |                   |                |                   |
| subjects affected / exposed | 4 / 133 (3.01%)   | 1 / 8 (12.50%) | 10 / 195 (5.13%)  |
| occurrences (all)           | 7                 | 1              | 10                |
| Pain in extremity           |                   |                |                   |
| subjects affected / exposed | 9 / 133 (6.77%)   | 0 / 8 (0.00%)  | 13 / 195 (6.67%)  |
| occurrences (all)           | 9                 | 0              | 14                |
| Neck pain                   |                   |                |                   |
| subjects affected / exposed | 1 / 133 (0.75%)   | 1 / 8 (12.50%) | 7 / 195 (3.59%)   |
| occurrences (all)           | 1                 | 1              | 8                 |
| Myalgia                     |                   |                |                   |
| subjects affected / exposed | 10 / 133 (7.52%)  | 0 / 8 (0.00%)  | 19 / 195 (9.74%)  |
| occurrences (all)           | 10                | 0              | 21                |
| Musculoskeletal pain        |                   |                |                   |
| subjects affected / exposed | 2 / 133 (1.50%)   | 1 / 8 (12.50%) | 5 / 195 (2.56%)   |
| occurrences (all)           | 2                 | 1              | 6                 |
| Musculoskeletal chest pain  |                   |                |                   |
| subjects affected / exposed | 2 / 133 (1.50%)   | 0 / 8 (0.00%)  | 11 / 195 (5.64%)  |
| occurrences (all)           | 2                 | 0              | 11                |
| Infections and infestations |                   |                |                   |
| Oral bacterial infection    |                   |                |                   |
| subjects affected / exposed | 0 / 133 (0.00%)   | 1 / 8 (12.50%) | 0 / 195 (0.00%)   |
| occurrences (all)           | 0                 | 1              | 0                 |
| Nasopharyngitis             |                   |                |                   |
| subjects affected / exposed | 3 / 133 (2.26%)   | 0 / 8 (0.00%)  | 14 / 195 (7.18%)  |
| occurrences (all)           | 3                 | 0              | 18                |
| Mucosal infection           |                   |                |                   |
| subjects affected / exposed | 0 / 133 (0.00%)   | 0 / 8 (0.00%)  | 1 / 195 (0.51%)   |
| occurrences (all)           | 0                 | 0              | 1                 |
| Eye infection               |                   |                |                   |

|                                    |                   |                |                   |
|------------------------------------|-------------------|----------------|-------------------|
| subjects affected / exposed        | 0 / 133 (0.00%)   | 0 / 8 (0.00%)  | 0 / 195 (0.00%)   |
| occurrences (all)                  | 0                 | 0              | 0                 |
| Conjunctivitis                     |                   |                |                   |
| subjects affected / exposed        | 3 / 133 (2.26%)   | 0 / 8 (0.00%)  | 4 / 195 (2.05%)   |
| occurrences (all)                  | 3                 | 0              | 4                 |
| Candida infection                  |                   |                |                   |
| subjects affected / exposed        | 0 / 133 (0.00%)   | 1 / 8 (12.50%) | 5 / 195 (2.56%)   |
| occurrences (all)                  | 0                 | 1              | 5                 |
| Bronchitis                         |                   |                |                   |
| subjects affected / exposed        | 1 / 133 (0.75%)   | 0 / 8 (0.00%)  | 3 / 195 (1.54%)   |
| occurrences (all)                  | 2                 | 0              | 3                 |
| Otitis externa                     |                   |                |                   |
| subjects affected / exposed        | 0 / 133 (0.00%)   | 1 / 8 (12.50%) | 0 / 195 (0.00%)   |
| occurrences (all)                  | 0                 | 1              | 0                 |
| Urinary tract infection            |                   |                |                   |
| subjects affected / exposed        | 31 / 133 (23.31%) | 0 / 8 (0.00%)  | 21 / 195 (10.77%) |
| occurrences (all)                  | 49                | 0              | 38                |
| Upper respiratory tract infection  |                   |                |                   |
| subjects affected / exposed        | 8 / 133 (6.02%)   | 0 / 8 (0.00%)  | 27 / 195 (13.85%) |
| occurrences (all)                  | 8                 | 0              | 37                |
| Tracheitis                         |                   |                |                   |
| subjects affected / exposed        | 0 / 133 (0.00%)   | 0 / 8 (0.00%)  | 0 / 195 (0.00%)   |
| occurrences (all)                  | 0                 | 0              | 0                 |
| Rhinitis                           |                   |                |                   |
| subjects affected / exposed        | 3 / 133 (2.26%)   | 0 / 8 (0.00%)  | 4 / 195 (2.05%)   |
| occurrences (all)                  | 5                 | 0              | 4                 |
| Respiratory tract infection        |                   |                |                   |
| subjects affected / exposed        | 2 / 133 (1.50%)   | 0 / 8 (0.00%)  | 7 / 195 (3.59%)   |
| occurrences (all)                  | 2                 | 0              | 7                 |
| Metabolism and nutrition disorders |                   |                |                   |
| Decreased appetite                 |                   |                |                   |
| subjects affected / exposed        | 32 / 133 (24.06%) | 2 / 8 (25.00%) | 48 / 195 (24.62%) |
| occurrences (all)                  | 35                | 2              | 59                |
| Hypophosphataemia                  |                   |                |                   |
| subjects affected / exposed        | 3 / 133 (2.26%)   | 1 / 8 (12.50%) | 20 / 195 (10.26%) |
| occurrences (all)                  | 5                 | 1              | 29                |

|                             |                   |                |                   |
|-----------------------------|-------------------|----------------|-------------------|
| Hyponatraemia               |                   |                |                   |
| subjects affected / exposed | 14 / 133 (10.53%) | 1 / 8 (12.50%) | 24 / 195 (12.31%) |
| occurrences (all)           | 20                | 1              | 38                |
| Hypokalaemia                |                   |                |                   |
| subjects affected / exposed | 15 / 133 (11.28%) | 1 / 8 (12.50%) | 20 / 195 (10.26%) |
| occurrences (all)           | 25                | 1              | 38                |
| Hypoalbuminaemia            |                   |                |                   |
| subjects affected / exposed | 16 / 133 (12.03%) | 0 / 8 (0.00%)  | 14 / 195 (7.18%)  |
| occurrences (all)           | 23                | 0              | 22                |
| Hyperglycaemia              |                   |                |                   |
| subjects affected / exposed | 9 / 133 (6.77%)   | 0 / 8 (0.00%)  | 16 / 195 (8.21%)  |
| occurrences (all)           | 19                | 0              | 27                |
| Hypercalcaemia              |                   |                |                   |
| subjects affected / exposed | 4 / 133 (3.01%)   | 0 / 8 (0.00%)  | 9 / 195 (4.62%)   |
| occurrences (all)           | 5                 | 0              | 10                |
| Dehydration                 |                   |                |                   |
| subjects affected / exposed | 3 / 133 (2.26%)   | 0 / 8 (0.00%)  | 9 / 195 (4.62%)   |
| occurrences (all)           | 4                 | 0              | 11                |
| Hypomagnesaemia             |                   |                |                   |
| subjects affected / exposed | 17 / 133 (12.78%) | 1 / 8 (12.50%) | 14 / 195 (7.18%)  |
| occurrences (all)           | 27                | 1              | 32                |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date            | Amendment                           |
|-----------------|-------------------------------------|
| 23 July 2015    | inclusion criteria updated          |
| 16 October 2015 | exclusion criteria update           |
| 16 March 2016   | study design update                 |
| 28 October 2016 | study design and arm cohorts update |
| 18 April 2018   | enrollment and study design update  |
| 18 July 2018    | enrollment and endpoints update     |
| 07 May 2019     | endpoints update                    |

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported