



## Clinical trial results:

### An Exploratory Study of the Biologic Effects of Nivolumab and Nivolumab in Combination with Ipilimumab Treatment in Subjects with Advanced Melanoma (Unresectable or Metastatic)

#### Summary

|                          |                 |
|--------------------------|-----------------|
| EudraCT number           | 2012-001840-23  |
| Trial protocol           | Outside EU/EEA  |
| Global end of trial date | 25 October 2018 |

#### Results information

|                                |              |
|--------------------------------|--------------|
| Result version number          | v1 (current) |
| This version publication date  | 25 June 2022 |
| First version publication date | 25 June 2022 |

#### Trial information

##### Trial identification

|                       |           |
|-----------------------|-----------|
| Sponsor protocol code | CA209-038 |
|-----------------------|-----------|

##### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT01621490 |
| WHO universal trial number (UTN)   | -           |

Notes:

#### Sponsors

|                              |   |
|------------------------------|---|
| Sponsor organisation name    | Bristol-Myers Squibb  |
| Sponsor organisation address | Chaussee de la Hulpe 18, 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                       | 21 March 2019   |
| Is this the analysis of the primary completion data? | No              |
| Global end of trial reached?                         | Yes             |
| Global end of trial date                             | 25 October 2018 |
| Was the trial ended prematurely?                     | No              |

Notes:

## General information about the trial

Main objective of the trial:

To investigate the pharmacodynamic activity of nivolumab, and nivolumab in combination with ipilimumab in the tumor environment and the periphery on biomarker measures such as circulating T cell subsets (activated and memory T cell populations by flow cytometry), interferon, interferon inducible factors and T cell (CD4 and CD8) infiltration in tumor biopsy sections from subjects with advanced melanoma.

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                          | 27 September 2012 |
| 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 | Netherlands: 20    |
| Country: Number of subjects enrolled | Spain: 26          |
| Country: Number of subjects enrolled | United States: 124 |
| Worldwide total number of subjects   | 170                |
| EEA total number of subjects         | 46                 |

Notes:

### Subjects enrolled per age group

|   |     |
|---|-----|
| In utero                                  | 0   |
| Preterm newborn - gestational age < 37 wk | 0   |
| Newborns (0-27 days)                      | 0   |
| Infants and toddlers (28 days-23 months)  | 0   |
| Children (2-11 years)                     | 0   |
| Adolescents (12-17 years)                 | 0   |
| Adults (18-64 years)                      | 122 |

|                     |    |
|---------------------|----|
| From 65 to 84 years | 47 |
| 85 years and over   | 1  |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

227 participants were enrolled; 55 did not enter the treatment period: 41 did not meet study criteria; 6 other; 5 withdrew consent; 1 adverse events; 2 deaths. 172 entered the treatment period. 2 were not treated; 1 received ipilimumab monotherapy prior to the closure of Arm C; 1 received an unplanned treatment; 168 were 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> | N3 60 M Naive |
|------------------|---------------|

Arm description:

Treatment Group: N3 = Nivolumab 3mg/kg; 60M = 60 minute infusion; Naive = Anti-CTLA4 Naive

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

Dosage and administration details:

Nivolumab 3 mg/kg administered intravenously (IV) in 60 minute infusion

|                  |             |
|------------------|-------------|
| <b>Arm title</b> | N3 60M Prog |
|------------------|-------------|

Arm description:

Treatment Group: N3 = Nivolumab 3mg/kg; 60M = 60 minute infusion; PROG = Anti-CTLA4 Progressed

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

Dosage and administration details:

Nivolumab 3 mg/kg administered intravenously (IV) in 60 minute infusion

|                  |                     |
|------------------|---------------------|
| <b>Arm title</b> | N1 60M + I3 90M, W2 |
|------------------|---------------------|

Arm description:

Treatment Group: N1 = Nivolumab 1mg/kg; I3 = Ipilimumab 3 mg/kg; 90M = 90 minute infusion; 60M = 60 minute infusion; W2 = Week 2 Biopsy

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

|   |                        |
|---|------------------------|
| Dosage and administration details:  |                        |
| Ipilimumab 3 mg/kg administered intravenously (IV) in 90 minute infusion  |                        |
| Investigational medicinal product name  | Nivolumab              |
| Investigational medicinal product code  |                        |
| Other name  |                        |
| Pharmaceutical forms  | Infusion               |
| Routes of administration  | Intravenous use        |
| Dosage and administration details:  |                        |
| Nivolumab 1 mg/kg administered intravenously (IV) in 60 minute infusion   |                        |
| <b>Arm title</b>  | N1 60M + I3 90M, W4    |
| Arm description:  |                        |
| Treatment Group: N1 = Nivolumab 1mg/kg; I3 = Ipilimumab 3 mg/kg; 90M = 90 minute infusion; 60M = 60 minute infusion; W4 = Week 4 Biopsy       |                        |
| Arm type  | Experimental           |
| Investigational medicinal product name  | Ipilimumab             |
| Investigational medicinal product code  |                        |
| Other name  |                        |
| Pharmaceutical forms  | Infusion               |
| Routes of administration  | Intravenous use        |
| Dosage and administration details:  |                        |
| Ipilimumab 3 mg/kg administered intravenously (IV) in 90 minute infusion  |                        |
| Investigational medicinal product name  | Nivolumab              |
| Investigational medicinal product code  |                        |
| Other name  |                        |
| Pharmaceutical forms  | Infusion               |
| Routes of administration  | Intravenous use        |
| Dosage and administration details:  |                        |
| Nivolumab 1 mg/kg administered intravenously (IV) in 60 minute infusion   |                        |
| <b>Arm title</b>  | N1 60M +I3 90M, WU     |
| Arm description:  |                        |
| Treatment Group: N1 = Nivolumab 1mg/kg; I3 = Ipilimumab 3 mg/kg; 90M = 90 minute infusion; 60M = 60 minute infusion; WU = Unknown Week Biopsy |                        |
| Arm type  | Experimental           |
| Investigational medicinal product name  | Ipilimumab             |
| Investigational medicinal product code  |                        |
| Other name  |                        |
| Pharmaceutical forms  | Infusion               |
| Routes of administration  | Intravenous use        |
| Dosage and administration details:  |                        |
| Ipilimumab 3 mg/kg administered intravenously (IV) in 90 minute infusion  |                        |
| Investigational medicinal product name  | Nivolumab              |
| Investigational medicinal product code  |                        |
| Other name  |                        |
| Pharmaceutical forms  | Infusion               |
| Routes of administration  | Intravenous use        |
| Dosage and administration details:  |                        |
| Nivolumab 1 mg/kg administered intravenously (IV) in 60 minute infusion   |                        |
| <b>Arm title</b>  | N1 30M + I3 30M non-BM |
| Arm description:  |                        |
| Treatment Group: N1 = Nivolumab 1mg/kg; I3 = Ipilimumab 3 mg/kg; 30M = 30 minute infusion; BM = Brain metastases                              |                        |
| Arm type  | Experimental           |

|  |                   |
|--|-------------------|
| Investigational medicinal product name   | Ipilimumab        |
| Investigational medicinal product code   |                   |
| Other name   |                   |
| Pharmaceutical forms   | Infusion          |
| Routes of administration   | Intravenous use   |
| Dosage and administration details:   |                   |
| Ipilimumab 3 mg/kg administered intravenously (IV) in 30 minute infusion   |                   |
| Investigational medicinal product name   | Nivolumab         |
| Investigational medicinal product code   |                   |
| Other name   |                   |
| Pharmaceutical forms   | Infusion          |
| Routes of administration   | Intravenous use   |
| Dosage and administration details:   |                   |
| Nivolumab 1 mg/kg administered intravenously (IV) in 30 minute infusion  |                   |
| <b>Arm title</b>   | N3 30M non-BM     |
| Arm description:   |                   |
| Treatment Group: N3 = Nivolumab 3mg/kg;30M = 30 minute infusion; BM = Brain metastases                           |                   |
| Arm type   | Experimental      |
| Investigational medicinal product name   | Nivolumab         |
| Investigational medicinal product code   |                   |
| Other name   |                   |
| Pharmaceutical forms   | Infusion          |
| Routes of administration   | Intravenous use   |
| Dosage and administration details:   |                   |
| Nivolumab 3 mg/kg administered intravenously (IV) in 30 minute infusion  |                   |
| <b>Arm title</b>   | N1 30M +I3 30M BM |
| Arm description:   |                   |
| Treatment Group: N1 = Nivolumab 1mg/kg; I3 = Ipilimumab 3 mg/kg; 30M = 30 minute infusion; BM = Brain metastases |                   |
| Arm type   | Experimental      |
| Investigational medicinal product name   | Nivolumab         |
| Investigational medicinal product code   |                   |
| Other name   |                   |
| Pharmaceutical forms   | Infusion          |
| Routes of administration   | Intravenous use   |
| Dosage and administration details:   |                   |
| Nivolumab 1 mg/kg administered intravenously (IV) in 30 minute infusion  |                   |
| Investigational medicinal product name   | Ipilimumab        |
| Investigational medicinal product code   |                   |
| Other name   |                   |
| Pharmaceutical forms   | Infusion          |
| Routes of administration   | Intravenous use   |
| Dosage and administration details:   |                   |
| Ipilimumab 3 mg/kg administered intravenously (IV) in 30 minute infusion   |                   |
| <b>Arm title</b>   | N3 30M BM         |
| Arm description:   |                   |
| Treatment Group: N3 = Nivolumab 3mg/kg; 30M = 30 minute infusion; BM = Brain metastases                          |                   |
| Arm type   | Experimental      |

|   |                 |
|---|-----------------|
| Investigational medicinal product name                                  | Nivolumab       |
| Investigational medicinal product code                                  |                 |
| Other name  |                 |
| Pharmaceutical forms  | Infusion        |
| Routes of administration  | Intravenous use |
| Dosage and administration details:                                      |                 |
| Nivolumab 3 mg/kg administered intravenously (IV) in 30 minute infusion |                 |
| <b>Arm title</b>  | I3 Monotherapy  |

Arm description:

Treatment Group: I3 = Ipilimumab 3 mg/kg infusion. Participant was enrolled prior to the closure of this arm via amendment

|  |                     |
|--|---------------------|
| Arm type   | Experimental        |
| Investigational medicinal product name             | Ipilimumab          |
| Investigational medicinal product code             |                     |
| Other name   |                     |
| Pharmaceutical forms                               | Infusion            |
| Routes of administration                           | Intravenous use     |
| Dosage and administration details:                 |                     |
| Ipilimumab 3 mg/kg administered intravenously (IV) |                     |
| <b>Arm title</b>                                   | Unplanned Treatment |

Arm description:

Unplanned treatment of nivolumab 1 mg/kg x 4 then nivolumab 3 mg/kg

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

Dosage and administration details:

Nivolumab 1 mg/kg administered intravenously (IV) for 4 doses followed by Nivolumab 3 mg/kg

| <b>Number of subjects in period 1</b> | N3 60 M Naive | N3 60M Prog | N1 60M + I3 90M, W2 |
|---------------------------------------|---------------|-------------|---------------------|
| Started                               | 41            | 44          | 11                  |
| Completed                             | 0             | 0           | 0                   |
| Not completed                         | 41            | 44          | 11                  |
| Adverse event, serious fatal          | -             | -           | -                   |
| Consent withdrawn by subject          | 1             | -           | -                   |
| Disease progression                   | 27            | 28          | 1                   |
| Completed                             | -             | -           | -                   |
| Study drug toxicity                   | 1             | 4           | 5                   |
| Subject request to discontinue study  | 1             | 3           | 1                   |
| Maximum clinical benefit              | 3             | 2           | -                   |
| Adverse event unrelated to study drug | 1             | 1           | -                   |
| Other reasons                         | 7             | 6           | 4                   |

|  |   |   |   |
|--|---|---|---|
| Subject no longer meets study criteria | - | - | - |
|--|---|---|---|

| Number of subjects in period 1         | N1 60M + I3 90M, W4 | N1 60M +I3 90M, WU | N1 30M + I3 30M non-BM |
|--|---------------------|--------------------|------------------------|
| Started                                | 10                  | 6                  | 25                     |
| Completed                              | 0                   | 0                  | 0                      |
| Not completed                          | 10                  | 6                  | 25                     |
| Adverse event, serious fatal           | -                   | -                  | -                      |
| Consent withdrawn by subject           | -                   | -                  | 1                      |
| Disease progression                    | 5                   | 3                  | 8                      |
| Completed                              | -                   | -                  | 1                      |
| Study drug toxicity                    | 3                   | 1                  | 10                     |
| Subject request to discontinue study   | 1                   | -                  | 2                      |
| Maximum clinical benefit               | -                   | -                  | -                      |
| Adverse event unrelated to study drug  | -                   | -                  | -                      |
| Other reasons                          | 1                   | 1                  | 3                      |
| Subject no longer meets study criteria | -                   | 1                  | -                      |

| Number of subjects in period 1         | N3 30M non-BM | N1 30M +I3 30M BM | N3 30M BM |
|--|---------------|-------------------|-----------|
| Started                                | 11            | 10                | 10        |
| Completed                              | 0             | 0                 | 0         |
| Not completed                          | 11            | 10                | 10        |
| Adverse event, serious fatal           | -             | -                 | 1         |
| Consent withdrawn by subject           | -             | -                 | -         |
| Disease progression                    | 7             | 1                 | 4         |
| Completed                              | -             | -                 | -         |
| Study drug toxicity                    | 1             | 4                 | 1         |
| Subject request to discontinue study   | 1             | -                 | 1         |
| Maximum clinical benefit               | 1             | 2                 | 2         |
| Adverse event unrelated to study drug  | -             | 2                 | -         |
| Other reasons                          | 1             | 1                 | 1         |
| Subject no longer meets study criteria | -             | -                 | -         |

| Number of subjects in period 1 | I3 Monotherapy | Unplanned Treatment |
|--------------------------------|----------------|---------------------|
| Started                        | 1              | 1                   |
| Completed                      | 0              | 0                   |
| Not completed                  | 1              | 1                   |
| Adverse event, serious fatal   | -              | -                   |
| Consent withdrawn by subject   | -              | -                   |
| Disease progression            | 1              | 1                   |



|  |   |   |
|--|---|---|
| Completed                              | - | - |
| Study drug toxicity                    | - | - |
| Subject request to discontinue study   | - | - |
| Maximum clinical benefit               | - | - |
| Adverse event unrelated to study drug  | - | - |
| Other reasons                          | - | - |
| Subject no longer meets study criteria | - | - |

## Baseline characteristics

| Reporting groups  |                        |
|---|------------------------|
| Reporting group title   | N3 60 M Naive          |
| Reporting group description:  |                        |
| Treatment Group: N3 = Nivolumab 3mg/kg; 60M = 60 minute infusion; Naive = Anti-CTLA4 Naive  |                        |
| Reporting group title   | N3 60M Prog            |
| Reporting group description:  |                        |
| Treatment Group: N3 = Nivolumab 3mg/kg; 60M = 60 minute infusion; PROG = Anti-CTLA4 Progressed  |                        |
| Reporting group title   | N1 60M + I3 90M, W2    |
| Reporting group description:  |                        |
| Treatment Group: N1 = Nivolumab 1mg/kg; I3 = Ipilimumab 3 mg/kg; 90M = 90 minute infusion; 60M = 60 minute infusion; W2 = Week 2 Biopsy       |                        |
| Reporting group title   | N1 60M + I3 90M, W4    |
| Reporting group description:  |                        |
| Treatment Group: N1 = Nivolumab 1mg/kg; I3 = Ipilimumab 3 mg/kg; 90M = 90 minute infusion; 60M = 60 minute infusion; W4 = Week 4 Biopsy       |                        |
| Reporting group title   | N1 60M +I3 90M, WU     |
| Reporting group description:  |                        |
| Treatment Group: N1 = Nivolumab 1mg/kg; I3 = Ipilimumab 3 mg/kg; 90M = 90 minute infusion; 60M = 60 minute infusion; WU = Unknown Week Biopsy |                        |
| Reporting group title   | N1 30M + I3 30M non-BM |
| Reporting group description:  |                        |
| Treatment Group: N1 = Nivolumab 1mg/kg; I3 = Ipilimumab 3 mg/kg; 30M = 30 minute infusion; BM = Brain metastases                              |                        |
| Reporting group title   | N3 30M non-BM          |
| Reporting group description:  |                        |
| Treatment Group: N3 = Nivolumab 3mg/kg;30M = 30 minute infusion; BM = Brain metastases  |                        |
| Reporting group title   | N1 30M +I3 30M BM      |
| Reporting group description:  |                        |
| Treatment Group: N1 = Nivolumab 1mg/kg; I3 = Ipilimumab 3 mg/kg; 30M = 30 minute infusion; BM = Brain metastases                              |                        |
| Reporting group title   | N3 30M BM              |
| Reporting group description:  |                        |
| Treatment Group: N3 = Nivolumab 3mg/kg; 30M = 30 minute infusion; BM = Brain metastases   |                        |
| Reporting group title   | I3 Monotherapy         |
| Reporting group description:  |                        |
| Treatment Group: I3 = Ipilimumab 3 mg/kg infusion. Participant was enrolled prior to the closure of this arm via amendment                    |                        |
| Reporting group title   | Unplanned Treatment    |
| Reporting group description:  |                        |
| Unplanned treatment of nivolumab 1 mg/kg x 4 then nivolumab 3 mg/kg   |                        |

| Reporting group values | N3 60 M Naive | N3 60M Prog | N1 60M + I3 90M, W2 |
|------------------------|---------------|-------------|---------------------|
| Number of subjects     | 41            | 44          | 11                  |
| Age categorical        |               |             |                     |
| Units: Subjects        |               |             |                     |
| Adults (18-64 years)   | 34            | 34          | 5                   |
| From 65-84 years       | 6             | 10          | 6                   |
| 85 years and over      | 1             | 0           | 0                   |

|   |         |         |         |
|---|---------|---------|---------|
| Age Continuous                            |         |         |         |
| "999"=N/A                                 |         |         |         |
| Units: years                              |         |         |         |
| arithmetic mean                           | 55.5    | 53.7    | 61.0    |
| standard deviation                        | ± 12.49 | ± 15.10 | ± 11.82 |
| Sex: Female, Male                         |         |         |         |
| Units:                                    |         |         |         |
| Female                                    | 19      | 18      | 3       |
| Male                                      | 22      | 26      | 8       |
| Race (NIH/OMB)                            |         |         |         |
| Units: Subjects                           |         |         |         |
| American Indian or Alaska Native          | 0       | 0       | 0       |
| Asian                                     | 0       | 1       | 0       |
| Native Hawaiian or Other Pacific Islander | 0       | 0       | 0       |
| Black or African American                 | 0       | 0       | 0       |
| White                                     | 41      | 43      | 11      |
| More than one race                        | 0       | 0       | 0       |
| Unknown or Not Reported                   | 0       | 0       | 0       |
| Ethnicity (NIH/OMB)                       |         |         |         |
| Units: Subjects                           |         |         |         |
| Hispanic or Latino                        | 2       | 0       | 2       |
| Not Hispanic or Latino                    | 34      | 41      | 6       |
| Unknown or Not Reported                   | 5       | 3       | 3       |

| <b>Reporting group values</b>             | N1 60M + I3 90M,<br>W4 | N1 60M +I3 90M,<br>WU | N1 30M + I3 30M<br>non-BM |
|---|------------------------|-----------------------|---------------------------|
| Number of subjects                        | 10                     | 6                     | 25                        |
| Age categorical                           |                        |                       |                           |
| Units: Subjects                           |                        |                       |                           |
| Adults (18-64 years)                      | 7                      | 4                     | 16                        |
| From 65-84 years                          | 3                      | 2                     | 9                         |
| 85 years and over                         | 0                      | 0                     | 0                         |
| Age Continuous                            |                        |                       |                           |
| "999"=N/A                                 |                        |                       |                           |
| Units: years                              |                        |                       |                           |
| arithmetic mean                           | 58.5                   | 56.8                  | 56.9                      |
| standard deviation                        | ± 13.29                | ± 9.64                | ± 13.52                   |
| Sex: Female, Male                         |                        |                       |                           |
| Units:                                    |                        |                       |                           |
| Female                                    | 4                      | 3                     | 8                         |
| Male                                      | 6                      | 3                     | 17                        |
| Race (NIH/OMB)                            |                        |                       |                           |
| Units: Subjects                           |                        |                       |                           |
| American Indian or Alaska Native          | 0                      | 0                     | 0                         |
| Asian                                     | 0                      | 0                     | 0                         |
| Native Hawaiian or Other Pacific Islander | 0                      | 0                     | 0                         |
| Black or African American                 | 0                      | 0                     | 0                         |
| White                                     | 10                     | 6                     | 25                        |
| More than one race                        | 0                      | 0                     | 0                         |
| Unknown or Not Reported                   | 0                      | 0                     | 0                         |
| Ethnicity (NIH/OMB)                       |                        |                       |                           |

|                         |    |   |    |
|-------------------------|----|---|----|
| Units: Subjects         |    |   |    |
| Hispanic or Latino      | 0  | 0 | 0  |
| Not Hispanic or Latino  | 10 | 5 | 15 |
| Unknown or Not Reported | 0  | 1 | 10 |

| Reporting group values                    | N3 30M non-BM | N1 30M +I3 30M BM | N3 30M BM |
|---|---------------|-------------------|-----------|
| Number of subjects                        | 11            | 10                | 10        |
| Age categorical                           |               |                   |           |
| Units: Subjects                           |               |                   |           |
| Adults (18-64 years)                      | 8             | 8                 | 5         |
| From 65-84 years                          | 3             | 2                 | 5         |
| 85 years and over                         | 0             | 0                 | 0         |
| Age Continuous                            |               |                   |           |
| "999"=N/A                                 |               |                   |           |
| Units: years                              |               |                   |           |
| arithmetic mean                           | 51.5          | 56.9              | 58.9      |
| standard deviation                        | ± 15.55       | ± 9.37            | ± 13.46   |
| Sex: Female, Male                         |               |                   |           |
| Units:                                    |               |                   |           |
| Female                                    | 4             | 4                 | 5         |
| Male                                      | 7             | 6                 | 5         |
| Race (NIH/OMB)                            |               |                   |           |
| Units: Subjects                           |               |                   |           |
| American Indian or Alaska Native          | 0             | 0                 | 0         |
| Asian                                     | 0             | 0                 | 0         |
| Native Hawaiian or Other Pacific Islander | 0             | 0                 | 0         |
| Black or African American                 | 0             | 0                 | 0         |
| White                                     | 11            | 10                | 10        |
| More than one race                        | 0             | 0                 | 0         |
| Unknown or Not Reported                   | 0             | 0                 | 0         |
| Ethnicity (NIH/OMB)                       |               |                   |           |
| Units: Subjects                           |               |                   |           |
| Hispanic or Latino                        | 1             | 1                 | 0         |
| Not Hispanic or Latino                    | 5             | 3                 | 7         |
| Unknown or Not Reported                   | 5             | 6                 | 3         |

| Reporting group values | I3 Monotherapy | Unplanned Treatment | Total |
|------------------------|----------------|---------------------|-------|
| Number of subjects     | 1              | 1                   | 170   |
| Age categorical        |                |                     |       |
| Units: Subjects        |                |                     |       |
| Adults (18-64 years)   | 1              | 0                   | 122   |
| From 65-84 years       | 0              | 1                   | 47    |
| 85 years and over      | 0              | 0                   | 1     |
| Age Continuous         |                |                     |       |
| "999"=N/A              |                |                     |       |
| Units: years           |                |                     |       |
| arithmetic mean        | 52.0           | 66.0                |       |
| standard deviation     | ± 999          | ± 999               | -     |

|   |   |   |     |
|---|---|---|-----|
| Sex: Female, Male                         |   |   |     |
| Units:                                    |   |   |     |
| Female                                    | 1 | 0 | 69  |
| Male                                      | 0 | 1 | 101 |
| Race (NIH/OMB)                            |   |   |     |
| Units: Subjects                           |   |   |     |
| American Indian or Alaska Native          | 0 | 0 | 0   |
| Asian                                     | 0 | 0 | 1   |
| Native Hawaiian or Other Pacific Islander | 0 | 0 | 0   |
| Black or African American                 | 0 | 0 | 0   |
| White                                     | 1 | 1 | 169 |
| More than one race                        | 0 | 0 | 0   |
| Unknown or Not Reported                   | 0 | 0 | 0   |
| Ethnicity (NIH/OMB)                       |   |   |     |
| Units: Subjects                           |   |   |     |
| Hispanic or Latino                        | 0 | 0 | 6   |
| Not Hispanic or Latino                    | 1 | 1 | 128 |
| Unknown or Not Reported                   | 0 | 0 | 36  |

### Subject analysis sets

|  |                    |
|--|--------------------|
| Subject analysis set title   | N3 60M Naive       |
| Subject analysis set type  | Sub-group analysis |
| Subject analysis set description:  |                    |
| Treatment Group: Part 1: Nivolumab 3 mg/kg 60 Minute Infusion Anti-CTLA4 Naive                                   |                    |
| Subject analysis set title   | N3 60M PROG        |
| Subject analysis set type  | Sub-group analysis |
| Subject analysis set description:  |                    |
| Treatment Group: N3 = Nivolumab 3mg/kg; 60M = 60 minute infusion; PROG = Anti-CTLA4 Progressed                   |                    |
| Subject analysis set title   | N1 60M + I3 90M    |
| Subject analysis set type  | Sub-group analysis |
| Subject analysis set description:  |                    |
| Treatment Group: Part 2: Nivolumab 1 mg/kg 60 Minute Infusion + Ipilimumab 3 mg/kg 90 Minute                     |                    |
| Subject analysis set title   | N1 30M + I3 30M BM |
| Subject analysis set type  | Sub-group analysis |
| Subject analysis set description:  |                    |
| Treatment Group: N1 = Nivolumab 1mg/kg; I3 = Ipilimumab 3 mg/kg; 30M = 30 minute infusion; BM = Brain metastases |                    |
| Subject analysis set title   | N1+ I3 Non-BM      |
| Subject analysis set type  | Sub-group analysis |
| Subject analysis set description:  |                    |
| Treatment Group: Part 2+3: Nivolumab 1 mg/kg + Ipilimumab 3 mg/kg Non-Brain Metastases                           |                    |
| Subject analysis set title   | Naive Nivo Mono    |
| Subject analysis set type  | Sub-group analysis |
| Subject analysis set description:  |                    |
| Nivolumab Monotherapy CTLA-4 Naive   |                    |
| Subject analysis set title   | All Nivo           |
| Subject analysis set type  | Sub-group analysis |
| Subject analysis set description:  |                    |
| Treatment Group: All Nivolumab Monotherapy   |                    |
| Subject analysis set title   | All Combo          |

|  |                            |
|--|----------------------------|
| Subject analysis set type  | Sub-group analysis         |
| Subject analysis set description:  |                            |
| Treatment Group: All Combination Therapy   |                            |
| Subject analysis set title   | Total                      |
| Subject analysis set type  | Sub-group analysis         |
| Subject analysis set description:  |                            |
| All treatments   |                            |
| Subject analysis set title   | N3 60M Naive               |
| Subject analysis set type  | Sub-group analysis         |
| Subject analysis set description:  |                            |
| Treatment Group: Part 1: Nivolumab 3 mg/kg 60 Minute Infusion Anti-CTLA4 Naive   |                            |
| Subject analysis set title   | N3 60M PROG                |
| Subject analysis set type  | Sub-group analysis         |
| Subject analysis set description:  |                            |
| Treatment Group: N3 = Nivolumab 3mg/kg; 60M = 60 minute infusion; PROG = Anti-CTLA4 Progressed                         |                            |
| Subject analysis set title   | N1 60M + I3 90M W2         |
| Subject analysis set type  | Sub-group analysis         |
| Subject analysis set description:  |                            |
| Treatment Group: Part 2: Nivolumab 1 mg/kg 60 Minute Infusion + Ipilimumab 3 mg/kg 90 Minute Infusion Week 2 Biopsy    |                            |
| Subject analysis set title   | N1 60M + I3 90M W4         |
| Subject analysis set type  | Sub-group analysis         |
| Subject analysis set description:  |                            |
| Treatment Group: Part 2: Nivolumab 1 mg/kg 60 Minute Infusion + Ipilimumab 3 mg/kg 90 Minute Infusion Week 4 Biopsy    |                            |
| Subject analysis set title   | N3 30M + I3 30M BM         |
| Subject analysis set type  | Sub-group analysis         |
| Subject analysis set description:  |                            |
| Treatment Group: Part 4: Nivolumab 1 mg/kg 30 Minute Infusion + Ipilimumab 3 mg/kg 30 Minute Infusion Brain Metastases |                            |
| Subject analysis set title   | Nivo Mono                  |
| Subject analysis set type  | Sub-group analysis         |
| Subject analysis set description:  |                            |
| Treatment Group: Part 1: Regular Infusion Nivolumab Mono   |                            |
| Subject analysis set title   | Nivo Mono Reduced Infusion |
| Subject analysis set type  | Sub-group analysis         |
| Subject analysis set description:  |                            |
| Treatment Group: Reduced Infusion Nivolumab Monotherapy  |                            |
| Subject analysis set title   | Week 2 Biopsy Combo        |
| Subject analysis set type  | Sub-group analysis         |
| Subject analysis set description:  |                            |
| Treatment Group: Week 2 Biopsy Combo   |                            |
| Subject analysis set title   | Week 2 Biopsy non-BM Combo |
| Subject analysis set type  | Sub-group analysis         |
| Subject analysis set description:  |                            |
| Treatment Group: Week 2 Biopsy Non-Brain Metastases Combo  |                            |
| Subject analysis set title   | Naive Nivo Mono non-BM     |
| Subject analysis set type  | Sub-group analysis         |
| Subject analysis set description:  |                            |
| Treatment Group: Naive Nivolumab Mono Non-Brain Metastases   |                            |
| Subject analysis set title   | N1 + I3 non-BM             |
| Subject analysis set type  | Sub-group analysis         |

Subject analysis set description:

Treatment Group: Part 2+3: Nivolumab 1 mg/kg + Ipilimumab 3 mg/kg Non-Brain Metastases

|                            |                    |
|----------------------------|--------------------|
| Subject analysis set title | N3 60M Naive       |
| Subject analysis set type  | Sub-group analysis |

Subject analysis set description:

N3 = Nivolumab 3mg/kg; 60M = 60 minute infusion; NAIVE = Anti-CTLA4 Naive

|                            |                    |
|----------------------------|--------------------|
| Subject analysis set title | N3 60M PROG        |
| Subject analysis set type  | Sub-group analysis |

Subject analysis set description:

Treatment Group: N3 = Nivolumab 3mg/kg; 60M = 60 minute infusion; PROG = Anti-CTLA4 Progressed

|                            |                    |
|----------------------------|--------------------|
| Subject analysis set title | N1 60M + I3 90M    |
| Subject analysis set type  | Sub-group analysis |

Subject analysis set description:

N1 = Nivolumab 1mg/kg; I3 = Ipilimumab 3 mg/kg; 90M = 90 minute infusion; 60M = 60 minute infusion

|                            |                    |
|----------------------------|--------------------|
| Subject analysis set title | N1 30M + I3 30M BM |
| Subject analysis set type  | Sub-group analysis |

Subject analysis set description:

Treatment Group: N1 = Nivolumab 1mg/kg; I3 = Ipilimumab 3 mg/kg; 30M = 30 minute infusion; BM = Brain metastases

|                            |                    |
|----------------------------|--------------------|
| Subject analysis set title | N3 60M Naive       |
| Subject analysis set type  | Sub-group analysis |

Subject analysis set description:

Part 1: Nivolumab 3 mg/kg 60 Minute Infusion Anti-CTLA4 Naive

|                            |                    |
|----------------------------|--------------------|
| Subject analysis set title | N1 60M + I3 90M    |
| Subject analysis set type  | Sub-group analysis |

Subject analysis set description:

Part 2: Nivolumab 1 mg/kg 60 Minute Infusion + Ipilimumab 3 mg/kg 90 Minute Infusion

|                            |                        |
|----------------------------|------------------------|
| Subject analysis set title | N1 30M + I3 30M Non-BM |
| Subject analysis set type  | Sub-group analysis     |

Subject analysis set description:

Part 3: Nivolumab 1 mg/kg 30 Minute Infusion + Ipilimumab 3 mg/kg 30 Minute Infusion Non-Brain Metastases

|                            |                    |
|----------------------------|--------------------|
| Subject analysis set title | N3 30M Non-BM      |
| Subject analysis set type  | Sub-group analysis |

Subject analysis set description:

Part 3: Nivolumab 3 mg/kg 30 Minute Infusion Non-Brain Metastases

|                            |                    |
|----------------------------|--------------------|
| Subject analysis set title | N1 30M I3 30M BM   |
| Subject analysis set type  | Sub-group analysis |

Subject analysis set description:

Part 4: Nivolumab 1 mg/kg 30 Minute Infusion + Ipilimumab 3 mg/kg 30 Minute Infusion Brain Metastases

|                            |                    |
|----------------------------|--------------------|
| Subject analysis set title | N3 60M NAIVE       |
| Subject analysis set type  | Sub-group analysis |

Subject analysis set description:

Treatment Group: N3 = Nivolumab 3mg/kg; 60M = 60 minute infusion; Naive = Anti-CTLA4 Naive

|                            |                    |
|----------------------------|--------------------|
| Subject analysis set title | N1 60M +I3 90M     |
| Subject analysis set type  | Sub-group analysis |

Subject analysis set description:

Treatment Group: N1 = Nivolumab 1mg/kg; I3 = Ipilimumab 3 mg/kg; 90M = 90 minute infusion; 60M = 60 minute infusion

|                            |                    |
|----------------------------|--------------------|
| Subject analysis set title | N3 60M NAIVE       |
| Subject analysis set type  | Sub-group analysis |

Subject analysis set description:

Treatment Group: N3 = Nivolumab 3mg/kg; 60M = 60 minute infusion; Naive = Anti-CTLA4 Naive

|                            |                    |
|----------------------------|--------------------|
| Subject analysis set title | N3 60M PROG        |
| Subject analysis set type  | Sub-group analysis |

Subject analysis set description:

Treatment Group: N3 = Nivolumab 3mg/kg; 60M = 60 minute infusion; PROG = Anti-CTLA4 Progressed

|                            |                    |
|----------------------------|--------------------|
| Subject analysis set title | N1 60M +I3 90M     |
| Subject analysis set type  | Sub-group analysis |

Subject analysis set description:

Treatment Group: N1 = Nivolumab 1mg/kg; I3 = Ipilimumab 3 mg/kg; 90M = 90 minute infusion; 60M = 60 minute infusion

|                            |                    |
|----------------------------|--------------------|
| Subject analysis set title | N1 60M+I3 90M      |
| Subject analysis set type  | Sub-group analysis |

Subject analysis set description:

N1 = Nivolumab 1mg/kg; I3 = Ipilimumab 3 mg/kg; 90M = 90 minute infusion; 60M = 60 minute infusion

|                            |                    |
|----------------------------|--------------------|
| Subject analysis set title | N1 30M + I3 30M BM |
| Subject analysis set type  | Sub-group analysis |

Subject analysis set description:

N3 = Nivolumab 3mg/kg; I3 = Ipilimumab 3 mg/kg; 30M = 30 minute infusion; BM = Brain metastases

|                            |                        |
|----------------------------|------------------------|
| Subject analysis set title | N1 30M + I3 30M NON-BM |
| Subject analysis set type  | Sub-group analysis     |

Subject analysis set description:

N1 = Nivolumab 1mg/kg; I3 = Ipilimumab 3 mg/kg; 30M = 30 minute infusion; BM = Brain metastases

|                            |                    |
|----------------------------|--------------------|
| Subject analysis set title | N3 30M NON-BM      |
| Subject analysis set type  | Sub-group analysis |

Subject analysis set description:

N3 = Nivolumab 3mg/kg; 30M = 30 minute infusion; BM = Brain metastases

|                            |                    |
|----------------------------|--------------------|
| Subject analysis set title | N3 60M NAIVE       |
| Subject analysis set type  | Sub-group analysis |

Subject analysis set description:

Treatment Group: N3 = Nivolumab 3mg/kg; 60M = 60 minute infusion; Naive = Anti-CTLA4 Naive

|                            |                    |
|----------------------------|--------------------|
| Subject analysis set title | N3 60M PROG        |
| Subject analysis set type  | Sub-group analysis |

Subject analysis set description:

Treatment Group: N3 = Nivolumab 3mg/kg; 60M = 60 minute infusion; PROG = Anti-CTLA4 Progressed

|                            |                       |
|----------------------------|-----------------------|
| Subject analysis set title | N1 60M + I3 (Nivo ADA |
| Subject analysis set type  | Sub-group analysis    |

Subject analysis set description:

Part 2: Nivolumab 1 mg/kg 60 Minute Infusion + Ipilimumab 3 mg/kg 90 Minute

|                            |                           |
|----------------------------|---------------------------|
| Subject analysis set title | N1 60M + I3 90M (Ipi ADA) |
| Subject analysis set type  | Sub-group analysis        |

Subject analysis set description:

Part 2: Nivolumab 1 mg/kg 60 Minute Infusion + Ipilimumab 3 mg/kg 90 Minute

|                            |                                   |
|----------------------------|-----------------------------------|
| Subject analysis set title | N1 30M + I3 30M Non-BM (Nivo ADA) |
| Subject analysis set type  | Sub-group analysis                |

Subject analysis set description:

Part 3: Nivolumab 1 mg/kg 30 Minute Infusion + Ipilimumab 3 mg/kg 30 Minute Infusion Non-Brain Metastases

|                            |                                  |
|----------------------------|----------------------------------|
| Subject analysis set title | N1 30M + I3 30M Non-BM (Ipi ADA) |
| Subject analysis set type  | Sub-group analysis               |

Subject analysis set description:

Part 3: Nivolumab 1 mg/kg 30 Minute Infusion + Ipilimumab 3 mg/kg 30 Minute Infusion Non-Brain



## Metastases

|  |                            |
|--|----------------------------|
| Subject analysis set title   | N1 30M + I3 30M (Nivo ADA) |
| Subject analysis set type  | Sub-group analysis         |
| Subject analysis set description:<br>Part 4: Nivolumab 1 mg/kg 30 Minute Infusion + Ipilimumab 3 mg/kg 30 Minute Infusion Brain Metastases   |                            |
| Subject analysis set title   | N1 30M + I3 30M (Ipi ADA)  |
| Subject analysis set type  | Sub-group analysis         |
| Subject analysis set description:<br>Part 4: Nivolumab 1 mg/kg 30 Minute Infusion + Ipilimumab 3 mg/kg 30 Minute Infusion Brain Metastases   |                            |
| Subject analysis set title   | Total (Nivo ADA)           |
| Subject analysis set type  | Sub-group analysis         |
| Subject analysis set description:<br>Total (All Nivolumab or Nivolumab + Ipilimumab Treated Subjects with Baseline and at Least One Post-Baseline Assessment)                      |                            |
| Subject analysis set title   | Total (Ipi ADA)            |
| Subject analysis set type  | Sub-group analysis         |
| Subject analysis set description:<br>Total (All Nivolumab or Nivolumab + Ipilimumab Treated Subjects with Baseline and at Least One Post-Baseline Assessment)                      |                            |
| Subject analysis set title   | N3 60M NAIVE, W4           |
| Subject analysis set type  | Sub-group analysis         |
| Subject analysis set description:<br>Treatment Group: N3 = Nivolumab 3mg/kg; 60M = 60 minute infusion; NAIVE = Anti-CTLA4 Naive  |                            |
| Subject analysis set title   | N3 60M PROG, W4            |
| Subject analysis set type  | Sub-group analysis         |
| Subject analysis set description:<br>Treatment Group: N3 = Nivolumab 3mg/kg; 60M = 60 minute infusion; PROG = Anti-CTLA4 Progressed;   |                            |
| Subject analysis set title   | N1 60M + I3 90M, WU        |
| Subject analysis set type  | Sub-group analysis         |
| Subject analysis set description:<br>Treatment Group: N1 = Nivolumab 1mg/kg; I3 = Ipilimumab 3 mg/kg; 90M = 90 minute infusion; 60M = 60 minute infusion; WU = Unknown Week Biopsy |                            |
| Subject analysis set title   | N1 30M + I3 30M NON-BM     |
| Subject analysis set type  | Sub-group analysis         |
| Subject analysis set description:<br>Treatment Group: N1 = Nivolumab 1mg/kg; I3 = Ipilimumab 3 mg/kg; 30M = 30 minute infusion; BM = Brain metastases                              |                            |
| Subject analysis set title   | N3 30M NON-BM, W2          |
| Subject analysis set type  | Sub-group analysis         |
| Subject analysis set description:<br>Treatment Group: N3 = Nivolumab 3mg/kg; 30M = 30 minute infusion; W2 = Week 2 Biopsy  |                            |
| Subject analysis set title   | N1 30M + I3 30M BM, W2     |
| Subject analysis set type  | Sub-group analysis         |
| Subject analysis set description:<br>Treatment Group: N1 = Nivolumab 1mg/kg; I3 = Ipilimumab 3 mg/kg; 30M = 30 minute infusion; W2 = Week 2 Biopsy                                 |                            |
| Subject analysis set title   | N3 30M BM, W2              |
| Subject analysis set type  | Sub-group analysis         |
| Subject analysis set description:<br>Treatment Group: N3 = Nivolumab 3mg/kg; 30M = 30 minute infusion; W2 = Week 2 Biopsy  |                            |
| Subject analysis set title   | N3 60M, W4                 |
| Subject analysis set type  | Sub-group analysis         |

Subject analysis set description:

N3 = Nivolumab 3mg/kg; 60M = 60 minute infusion; W4 = Week 4 Biopsy

|                            |                    |
|----------------------------|--------------------|
| Subject analysis set title | N3 30M, W2         |
| Subject analysis set type  | Sub-group analysis |

Subject analysis set description:

Treatment Group: N3 = Nivolumab 3mg/kg; 30M = 30 minute infusion; W2 = Week 2 Biopsy

|                            |                    |
|----------------------------|--------------------|
| Subject analysis set title | N1 + I3, W2        |
| Subject analysis set type  | Sub-group analysis |

Subject analysis set description:

N1 = Nivolumab 1mg/kg; I3 = Ipilimumab 3 mg/kg; W2 = Week 2 Biopsy

|                            |                    |
|----------------------------|--------------------|
| Subject analysis set title | N1 + I3 W2, NON-BM |
| Subject analysis set type  | Sub-group analysis |

Subject analysis set description:

N1 = Nivolumab 1mg/kg; I3 = Ipilimumab 3 mg/kg; W2 = Week 2 Biopsy; BM = Brain metastases

|                            |                    |
|----------------------------|--------------------|
| Subject analysis set title | N3 NAIVE, NON-BM   |
| Subject analysis set type  | Sub-group analysis |

Subject analysis set description:

N3 = Nivolumab 3mg/kg; NAIVE = Anti-CTLA4 Naive; BM = Brain metastases

|                            |                    |
|----------------------------|--------------------|
| Subject analysis set title | N1 + I3 NON-BM     |
| Subject analysis set type  | Sub-group analysis |

Subject analysis set description:

N1 = Nivolumab 1mg/kg; I3 = Ipilimumab 3 mg/kg; BM = Brain metastases

|                            |                    |
|----------------------------|--------------------|
| Subject analysis set title | Total              |
| Subject analysis set type  | Sub-group analysis |

Subject analysis set description:

All treatments

|                            |                    |
|----------------------------|--------------------|
| Subject analysis set title | N1 + I3 NON-BM     |
| Subject analysis set type  | Sub-group analysis |

Subject analysis set description:

N1 = Nivolumab 1mg/kg; I3 = Ipilimumab 3 mg/kg; BM = Brain metastases

|                            |                    |
|----------------------------|--------------------|
| Subject analysis set title | N3 NAIVE           |
| Subject analysis set type  | Sub-group analysis |

Subject analysis set description:

N3 = Nivolumab 3mg/kg; NAIVE = Anti-CTLA4 Naive

|                            |                    |
|----------------------------|--------------------|
| Subject analysis set title | All N3             |
| Subject analysis set type  | Sub-group analysis |

Subject analysis set description:

N3 = Nivolumab 3mg/kg

|                            |                    |
|----------------------------|--------------------|
| Subject analysis set title | N1 + I3            |
| Subject analysis set type  | Sub-group analysis |

Subject analysis set description:

All combination

|                            |                    |
|----------------------------|--------------------|
| Subject analysis set title | Total              |
| Subject analysis set type  | Sub-group analysis |

Subject analysis set description:

All treatments

|                               |              |             |                 |
|-------------------------------|--------------|-------------|-----------------|
| <b>Reporting group values</b> | N3 60M Naive | N3 60M PROG | N1 60M + I3 90M |
| Number of subjects            | 40           | 40          | 27              |

|   |   |   |   |
|---|---|---|---|
| Age categorical                           |   |   |   |
| Units: Subjects                           |   |   |   |
| Adults (18-64 years)                      |   |   |   |
| From 65-84 years                          |   |   |   |
| 85 years and over                         |   |   |   |
| Age Continuous                            |   |   |   |
| "999"=N/A                                 |   |   |   |
| Units: years                              |   |   |   |
| arithmetic mean                           |   |   |   |
| standard deviation                        | ± | ± | ± |
| Sex: Female, Male                         |   |   |   |
| Units:                                    |   |   |   |
| Female                                    |   |   |   |
| Male                                      |   |   |   |
| Race (NIH/OMB)                            |   |   |   |
| Units: Subjects                           |   |   |   |
| American Indian or Alaska Native          |   |   |   |
| Asian                                     |   |   |   |
| Native Hawaiian or Other Pacific Islander |   |   |   |
| Black or African American                 |   |   |   |
| White                                     |   |   |   |
| More than one race                        |   |   |   |
| Unknown or Not Reported                   |   |   |   |
| Ethnicity (NIH/OMB)                       |   |   |   |
| Units: Subjects                           |   |   |   |
| Hispanic or Latino                        |   |   |   |
| Not Hispanic or Latino                    |   |   |   |
| Unknown or Not Reported                   |   |   |   |

| <b>Reporting group values</b>    | N1 30M + I3 30M<br>BM | N1+ I3 Non-BM | Naive Nivo Mono |
|----------------------------------|-----------------------|---------------|-----------------|
| Number of subjects               | 8                     | 50            | 58              |
| Age categorical                  |                       |               |                 |
| Units: Subjects                  |                       |               |                 |
| Adults (18-64 years)             |                       |               |                 |
| From 65-84 years                 |                       |               |                 |
| 85 years and over                |                       |               |                 |
| Age Continuous                   |                       |               |                 |
| "999"=N/A                        |                       |               |                 |
| Units: years                     |                       |               |                 |
| arithmetic mean                  |                       |               |                 |
| standard deviation               | ±                     | ±             | ±               |
| Sex: Female, Male                |                       |               |                 |
| Units:                           |                       |               |                 |
| Female                           |                       |               |                 |
| Male                             |                       |               |                 |
| Race (NIH/OMB)                   |                       |               |                 |
| Units: Subjects                  |                       |               |                 |
| American Indian or Alaska Native |                       |               |                 |
| Asian                            |                       |               |                 |

|   |  |  |  |
|---|--|--|--|
| Native Hawaiian or Other Pacific Islander |  |  |  |
| Black or African American                 |  |  |  |
| White                                     |  |  |  |
| More than one race                        |  |  |  |
| Unknown or Not Reported                   |  |  |  |
| Ethnicity (NIH/OMB)                       |  |  |  |
| Units: Subjects                           |  |  |  |
| Hispanic or Latino                        |  |  |  |
| Not Hispanic or Latino                    |  |  |  |
| Unknown or Not Reported                   |  |  |  |

| Reporting group values                    | All Nivo | All Combo | Total |
|---|----------|-----------|-------|
| Number of subjects                        | 98       | 58        | 156   |
| Age categorical                           |          |           |       |
| Units: Subjects                           |          |           |       |
| Adults (18-64 years)                      |          |           |       |
| From 65-84 years                          |          |           |       |
| 85 years and over                         |          |           |       |
| Age Continuous                            |          |           |       |
| "999"=N/A                                 |          |           |       |
| Units: years                              |          |           |       |
| arithmetic mean                           |          |           |       |
| standard deviation                        | ±        | ±         | ±     |
| Sex: Female, Male                         |          |           |       |
| Units:                                    |          |           |       |
| Female                                    |          |           |       |
| Male                                      |          |           |       |
| Race (NIH/OMB)                            |          |           |       |
| Units: Subjects                           |          |           |       |
| American Indian or Alaska Native          |          |           |       |
| Asian                                     |          |           |       |
| Native Hawaiian or Other Pacific Islander |          |           |       |
| Black or African American                 |          |           |       |
| White                                     |          |           |       |
| More than one race                        |          |           |       |
| Unknown or Not Reported                   |          |           |       |
| Ethnicity (NIH/OMB)                       |          |           |       |
| Units: Subjects                           |          |           |       |
| Hispanic or Latino                        |          |           |       |
| Not Hispanic or Latino                    |          |           |       |
| Unknown or Not Reported                   |          |           |       |

| Reporting group values | N3 60M Naive | N3 60M PROG | N1 60M + I3 90M W2 |
|------------------------|--------------|-------------|--------------------|
| Number of subjects     | 25           | 23          | 11                 |
| Age categorical        |              |             |                    |
| Units: Subjects        |              |             |                    |
| Adults (18-64 years)   |              |             |                    |
| From 65-84 years       |              |             |                    |
| 85 years and over      |              |             |                    |

|   |       |       |       |
|---|-------|-------|-------|
| Age Continuous  |       |       |       |
| "999"=N/A   |       |       |       |
| Units: years<br>arithmetic mean<br>standard deviation   | $\pm$ | $\pm$ | $\pm$ |
| Sex: Female, Male   |       |       |       |
| Units:  |       |       |       |
| Female<br>Male  |       |       |       |
| Race (NIH/OMB)  |       |       |       |
| Units: Subjects   |       |       |       |
| American Indian or Alaska Native<br>Asian<br>Native Hawaiian or Other Pacific Islander<br>Black or African American<br>White<br>More than one race<br>Unknown or Not Reported |       |       |       |
| Ethnicity (NIH/OMB)   |       |       |       |
| Units: Subjects   |       |       |       |
| Hispanic or Latino<br>Not Hispanic or Latino<br>Unknown or Not Reported   |       |       |       |

| <b>Reporting group values</b>   | N1 60M + I3 90M<br>W4 | N3 30M + I3 30M<br>BM | Nivo Mono |
|---|-----------------------|-----------------------|-----------|
| Number of subjects  | 10                    | 3                     | 48        |
| Age categorical   |                       |                       |           |
| Units: Subjects   |                       |                       |           |
| Adults (18-64 years)<br>From 65-84 years<br>85 years and over   |                       |                       |           |
| Age Continuous  |                       |                       |           |
| "999"=N/A   |                       |                       |           |
| Units: years<br>arithmetic mean<br>standard deviation   | $\pm$                 | $\pm$                 | $\pm$     |
| Sex: Female, Male   |                       |                       |           |
| Units:  |                       |                       |           |
| Female<br>Male  |                       |                       |           |
| Race (NIH/OMB)  |                       |                       |           |
| Units: Subjects   |                       |                       |           |
| American Indian or Alaska Native<br>Asian<br>Native Hawaiian or Other Pacific Islander<br>Black or African American<br>White<br>More than one race<br>Unknown or Not Reported |                       |                       |           |
| Ethnicity (NIH/OMB)   |                       |                       |           |

|                         |  |  |  |
|-------------------------|--|--|--|
| Units: Subjects         |  |  |  |
| Hispanic or Latino      |  |  |  |
| Not Hispanic or Latino  |  |  |  |
| Unknown or Not Reported |  |  |  |

| Reporting group values                    | Nivo Mono Reduced Infusion | Week 2 Biopsy Combo | Week 2 Biopsy non-BM Combo |
|---|----------------------------|---------------------|----------------------------|
| Number of subjects                        | 12                         | 29                  | 26                         |
| Age categorical                           |                            |                     |                            |
| Units: Subjects                           |                            |                     |                            |
| Adults (18-64 years)                      |                            |                     |                            |
| From 65-84 years                          |                            |                     |                            |
| 85 years and over                         |                            |                     |                            |
| Age Continuous                            |                            |                     |                            |
| "999"=N/A                                 |                            |                     |                            |
| Units: years                              |                            |                     |                            |
| arithmetic mean                           |                            |                     |                            |
| standard deviation                        | ±                          | ±                   | ±                          |
| Sex: Female, Male                         |                            |                     |                            |
| Units:                                    |                            |                     |                            |
| Female                                    |                            |                     |                            |
| Male                                      |                            |                     |                            |
| Race (NIH/OMB)                            |                            |                     |                            |
| Units: Subjects                           |                            |                     |                            |
| American Indian or Alaska Native          |                            |                     |                            |
| Asian                                     |                            |                     |                            |
| Native Hawaiian or Other Pacific Islander |                            |                     |                            |
| Black or African American                 |                            |                     |                            |
| White                                     |                            |                     |                            |
| More than one race                        |                            |                     |                            |
| Unknown or Not Reported                   |                            |                     |                            |
| Ethnicity (NIH/OMB)                       |                            |                     |                            |
| Units: Subjects                           |                            |                     |                            |
| Hispanic or Latino                        |                            |                     |                            |
| Not Hispanic or Latino                    |                            |                     |                            |
| Unknown or Not Reported                   |                            |                     |                            |

| Reporting group values | Naive Nivo Mono non-BM | N1 + I3 non-BM | N3 60M Naive |
|------------------------|------------------------|----------------|--------------|
| Number of subjects     | 35                     | 40             | 41           |
| Age categorical        |                        |                |              |
| Units: Subjects        |                        |                |              |
| Adults (18-64 years)   |                        |                |              |
| From 65-84 years       |                        |                |              |
| 85 years and over      |                        |                |              |
| Age Continuous         |                        |                |              |
| "999"=N/A              |                        |                |              |
| Units: years           |                        |                |              |
| arithmetic mean        |                        |                |              |
| standard deviation     | ±                      | ±              | ±            |

|   |  |  |  |
|---|--|--|--|
| Sex: Female, Male<br>Units:               |  |  |  |
| Female                                    |  |  |  |
| Male                                      |  |  |  |
| Race (NIH/OMB)<br>Units: Subjects         |  |  |  |
| American Indian or Alaska Native          |  |  |  |
| Asian                                     |  |  |  |
| Native Hawaiian or Other Pacific Islander |  |  |  |
| Black or African American                 |  |  |  |
| White                                     |  |  |  |
| More than one race                        |  |  |  |
| Unknown or Not Reported                   |  |  |  |
| Ethnicity (NIH/OMB)<br>Units: Subjects    |  |  |  |
| Hispanic or Latino                        |  |  |  |
| Not Hispanic or Latino                    |  |  |  |
| Unknown or Not Reported                   |  |  |  |

| <b>Reporting group values</b>             | N3 60M PROG | N1 60M + I3 90M | N1 30M + I3 30M<br>BM |
|---|-------------|-----------------|-----------------------|
| Number of subjects                        | 44          | 27              | 10                    |
| Age categorical<br>Units: Subjects        |             |                 |                       |
| Adults (18-64 years)                      |             |                 |                       |
| From 65-84 years                          |             |                 |                       |
| 85 years and over                         |             |                 |                       |
| Age Continuous                            |             |                 |                       |
| "999"=N/A                                 |             |                 |                       |
| Units: years                              |             |                 |                       |
| arithmetic mean                           |             |                 |                       |
| standard deviation                        | ±           | ±               | ±                     |
| Sex: Female, Male<br>Units:               |             |                 |                       |
| Female                                    |             |                 |                       |
| Male                                      |             |                 |                       |
| Race (NIH/OMB)<br>Units: Subjects         |             |                 |                       |
| American Indian or Alaska Native          |             |                 |                       |
| Asian                                     |             |                 |                       |
| Native Hawaiian or Other Pacific Islander |             |                 |                       |
| Black or African American                 |             |                 |                       |
| White                                     |             |                 |                       |
| More than one race                        |             |                 |                       |
| Unknown or Not Reported                   |             |                 |                       |
| Ethnicity (NIH/OMB)<br>Units: Subjects    |             |                 |                       |
| Hispanic or Latino                        |             |                 |                       |
| Not Hispanic or Latino                    |             |                 |                       |
| Unknown or Not Reported                   |             |                 |                       |

| <b>Reporting group values</b>  | N3 60M Naive | N1 60M + I3 90M | N1 30M + I3 30M<br>Non-BM |
|--|--------------|-----------------|---------------------------|
| Number of subjects   | 41           | 27              | 25                        |
| Age categorical<br>Units: Subjects   |              |                 |                           |
| Adults (18-64 years)<br>From 65-84 years<br>85 years and over  |              |                 |                           |
| Age Continuous   |              |                 |                           |
| "999"=N/A  |              |                 |                           |
| Units: years<br>arithmetic mean<br>standard deviation  | ±            | ±               | ±                         |
| Sex: Female, Male<br>Units:  |              |                 |                           |
| Female<br>Male   |              |                 |                           |
| Race (NIH/OMB)<br>Units: Subjects  |              |                 |                           |
| American Indian or Alaska Native<br>Asian<br>Native Hawaiian or Other Pacific<br>Islander<br>Black or African American<br>White<br>More than one race<br>Unknown or Not Reported |              |                 |                           |
| Ethnicity (NIH/OMB)<br>Units: Subjects   |              |                 |                           |
| Hispanic or Latino<br>Not Hispanic or Latino<br>Unknown or Not Reported  |              |                 |                           |

| <b>Reporting group values</b>                                 | N3 30M Non-BM | N1 30M I3 30M BM | N3 60M NAIVE |
|---|---------------|------------------|--------------|
| Number of subjects  | 11            | 10               | 41           |
| Age categorical<br>Units: Subjects                            |               |                  |              |
| Adults (18-64 years)<br>From 65-84 years<br>85 years and over |               |                  |              |
| Age Continuous  |               |                  |              |
| "999"=N/A   |               |                  |              |
| Units: years<br>arithmetic mean<br>standard deviation         | ±             | ±                | ±            |
| Sex: Female, Male<br>Units:                                   |               |                  |              |
| Female<br>Male  |               |                  |              |
| Race (NIH/OMB)<br>Units: Subjects                             |               |                  |              |
| American Indian or Alaska Native                              |               |                  |              |



|   |  |  |  |
|---|--|--|--|
| Asian<br>Native Hawaiian or Other Pacific Islander<br>Black or African American<br>White<br>More than one race<br>Unknown or Not Reported |  |  |  |
| Ethnicity (NIH/OMB)<br>Units: Subjects  |  |  |  |
| Hispanic or Latino<br>Not Hispanic or Latino<br>Unknown or Not Reported   |  |  |  |

| Reporting group values  | N1 60M +I3 90M | N3 60M NAIVE | N3 60M PROG |
|---|----------------|--------------|-------------|
| Number of subjects  | 27             | 29           | 33          |
| Age categorical<br>Units: Subjects  |                |              |             |
| Adults (18-64 years)<br>From 65-84 years<br>85 years and over   |                |              |             |
| Age Continuous  |                |              |             |
| "999"=N/A   |                |              |             |
| Units: years<br>arithmetic mean<br>standard deviation   | ±              | ±            | ±           |
| Sex: Female, Male<br>Units:   |                |              |             |
| Female<br>Male  |                |              |             |
| Race (NIH/OMB)<br>Units: Subjects   |                |              |             |
| American Indian or Alaska Native<br>Asian<br>Native Hawaiian or Other Pacific Islander<br>Black or African American<br>White<br>More than one race<br>Unknown or Not Reported |                |              |             |
| Ethnicity (NIH/OMB)<br>Units: Subjects  |                |              |             |
| Hispanic or Latino<br>Not Hispanic or Latino<br>Unknown or Not Reported   |                |              |             |

| Reporting group values                   | N1 60M +I3 90M | N1 60M+I3 90M | N1 30M + I3 30M BM |
|--|----------------|---------------|--------------------|
| Number of subjects                       | 21             | 27            | 10                 |
| Age categorical<br>Units: Subjects       |                |               |                    |
| Adults (18-64 years)<br>From 65-84 years |                |               |                    |

|                   |  |  |  |
|-------------------|--|--|--|
| 85 years and over |  |  |  |
|-------------------|--|--|--|

|   |   |      |      |
|---|---|------|------|
| Age Continuous                            |   |      |      |
| "999"=N/A                                 |   |      |      |
| Units: years                              |   |      |      |
| arithmetic mean                           |   | 44.4 | 70.0 |
| standard deviation                        | ± | ±    | ±    |
| Sex: Female, Male                         |   |      |      |
| Units:                                    |   |      |      |
| Female                                    |   |      |      |
| Male                                      |   |      |      |
| Race (NIH/OMB)                            |   |      |      |
| Units: Subjects                           |   |      |      |
| American Indian or Alaska Native          |   |      |      |
| Asian                                     |   |      |      |
| Native Hawaiian or Other Pacific Islander |   |      |      |
| Black or African American                 |   |      |      |
| White                                     |   |      |      |
| More than one race                        |   |      |      |
| Unknown or Not Reported                   |   |      |      |
| Ethnicity (NIH/OMB)                       |   |      |      |
| Units: Subjects                           |   |      |      |
| Hispanic or Latino                        |   |      |      |
| Not Hispanic or Latino                    |   |      |      |
| Unknown or Not Reported                   |   |      |      |

| Reporting group values                    | N1 30M + I3 30M<br>NON-BM | N3 30M NON-BM | N3 60M NAIVE |
|---|---------------------------|---------------|--------------|
| Number of subjects                        | 25                        | 11            | 38           |
| Age categorical                           |                           |               |              |
| Units: Subjects                           |                           |               |              |
| Adults (18-64 years)                      |                           |               |              |
| From 65-84 years                          |                           |               |              |
| 85 years and over                         |                           |               |              |
| Age Continuous                            |                           |               |              |
| "999"=N/A                                 |                           |               |              |
| Units: years                              |                           |               |              |
| arithmetic mean                           | 26.25                     |               |              |
| standard deviation                        | ±                         | ±             | ±            |
| Sex: Female, Male                         |                           |               |              |
| Units:                                    |                           |               |              |
| Female                                    |                           |               |              |
| Male                                      |                           |               |              |
| Race (NIH/OMB)                            |                           |               |              |
| Units: Subjects                           |                           |               |              |
| American Indian or Alaska Native          |                           |               |              |
| Asian                                     |                           |               |              |
| Native Hawaiian or Other Pacific Islander |                           |               |              |
| Black or African American                 |                           |               |              |

|   |  |  |  |
|---|--|--|--|
| White<br>More than one race<br>Unknown or Not Reported                  |  |  |  |
| Ethnicity (NIH/OMB)<br>Units: Subjects                                  |  |  |  |
| Hispanic or Latino<br>Not Hispanic or Latino<br>Unknown or Not Reported |  |  |  |

| Reporting group values  | N3 60M PROG | N1 60M + I3 (Nivo ADA) | N1 60M + I3 90M (Ipi ADA) |
|---|-------------|------------------------|---------------------------|
| Number of subjects  | 42          | 22                     | 22                        |
| Age categorical<br>Units: Subjects  |             |                        |                           |
| Adults (18-64 years)<br>From 65-84 years<br>85 years and over   |             |                        |                           |
| Age Continuous  |             |                        |                           |
| "999"=N/A   |             |                        |                           |
| Units: years<br>arithmetic mean<br>standard deviation   | ±           | ±                      | ±                         |
| Sex: Female, Male<br>Units:   |             |                        |                           |
| Female<br>Male  |             |                        |                           |
| Race (NIH/OMB)<br>Units: Subjects   |             |                        |                           |
| American Indian or Alaska Native<br>Asian<br>Native Hawaiian or Other Pacific Islander<br>Black or African American<br>White<br>More than one race<br>Unknown or Not Reported |             |                        |                           |
| Ethnicity (NIH/OMB)<br>Units: Subjects  |             |                        |                           |
| Hispanic or Latino<br>Not Hispanic or Latino<br>Unknown or Not Reported   |             |                        |                           |

| Reporting group values  | N1 30M + I3 30M Non-BM (Nivo ADA) | N1 30M + I3 30M Non-BM (Ipi ADA) | N1 30M + I3 30M (Nivo ADA) |
|---|-----------------------------------|----------------------------------|----------------------------|
| Number of subjects  | 24                                | 23                               | 10                         |
| Age categorical<br>Units: Subjects                            |                                   |                                  |                            |
| Adults (18-64 years)<br>From 65-84 years<br>85 years and over |                                   |                                  |                            |

|   |       |       |       |
|---|-------|-------|-------|
| Age Continuous  |       |       |       |
| "999"=N/A   |       |       |       |
| Units: years<br>arithmetic mean<br>standard deviation   | $\pm$ | $\pm$ | $\pm$ |
| Sex: Female, Male   |       |       |       |
| Units:  |       |       |       |
| Female<br>Male  |       |       |       |
| Race (NIH/OMB)  |       |       |       |
| Units: Subjects   |       |       |       |
| American Indian or Alaska Native<br>Asian<br>Native Hawaiian or Other Pacific Islander<br>Black or African American<br>White<br>More than one race<br>Unknown or Not Reported |       |       |       |
| Ethnicity (NIH/OMB)   |       |       |       |
| Units: Subjects   |       |       |       |
| Hispanic or Latino<br>Not Hispanic or Latino<br>Unknown or Not Reported   |       |       |       |

| <b>Reporting group values</b>   | N1 30M + I3 30M<br>(Ipi ADA) | Total (Nivo ADA) | Total (Ipi ADA) |
|---|------------------------------|------------------|-----------------|
| Number of subjects  | 9                            | 154              | 54              |
| Age categorical   |                              |                  |                 |
| Units: Subjects   |                              |                  |                 |
| Adults (18-64 years)<br>From 65-84 years<br>85 years and over   |                              |                  |                 |
| Age Continuous  |                              |                  |                 |
| "999"=N/A   |                              |                  |                 |
| Units: years<br>arithmetic mean<br>standard deviation   | $\pm$                        | $\pm$            | $\pm$           |
| Sex: Female, Male   |                              |                  |                 |
| Units:  |                              |                  |                 |
| Female<br>Male  |                              |                  |                 |
| Race (NIH/OMB)  |                              |                  |                 |
| Units: Subjects   |                              |                  |                 |
| American Indian or Alaska Native<br>Asian<br>Native Hawaiian or Other Pacific Islander<br>Black or African American<br>White<br>More than one race<br>Unknown or Not Reported |                              |                  |                 |
| Ethnicity (NIH/OMB)   |                              |                  |                 |

|                         |  |  |  |
|-------------------------|--|--|--|
| Units: Subjects         |  |  |  |
| Hispanic or Latino      |  |  |  |
| Not Hispanic or Latino  |  |  |  |
| Unknown or Not Reported |  |  |  |

| Reporting group values                    | N3 60M NAIVE, W4 | N3 60M PROG, W4 | N1 60M + I3 90M, WU |
|---|------------------|-----------------|---------------------|
| Number of subjects                        | 39               | 36              | 6                   |
| Age categorical                           |                  |                 |                     |
| Units: Subjects                           |                  |                 |                     |
| Adults (18-64 years)                      |                  |                 |                     |
| From 65-84 years                          |                  |                 |                     |
| 85 years and over                         |                  |                 |                     |
| Age Continuous                            |                  |                 |                     |
| "999"=N/A                                 |                  |                 |                     |
| Units: years                              |                  |                 |                     |
| arithmetic mean                           |                  |                 |                     |
| standard deviation                        | ±                | ±               | ±                   |
| Sex: Female, Male                         |                  |                 |                     |
| Units:                                    |                  |                 |                     |
| Female                                    |                  |                 |                     |
| Male                                      |                  |                 |                     |
| Race (NIH/OMB)                            |                  |                 |                     |
| Units: Subjects                           |                  |                 |                     |
| American Indian or Alaska Native          |                  |                 |                     |
| Asian                                     |                  |                 |                     |
| Native Hawaiian or Other Pacific Islander |                  |                 |                     |
| Black or African American                 |                  |                 |                     |
| White                                     |                  |                 |                     |
| More than one race                        |                  |                 |                     |
| Unknown or Not Reported                   |                  |                 |                     |
| Ethnicity (NIH/OMB)                       |                  |                 |                     |
| Units: Subjects                           |                  |                 |                     |
| Hispanic or Latino                        |                  |                 |                     |
| Not Hispanic or Latino                    |                  |                 |                     |
| Unknown or Not Reported                   |                  |                 |                     |

| Reporting group values | N1 30M + I3 30M NON-BM | N3 30M NON-BM, W2 | N1 30M + I3 30M BM, W2 |
|------------------------|------------------------|-------------------|------------------------|
| Number of subjects     | 22                     | 9                 | 4                      |
| Age categorical        |                        |                   |                        |
| Units: Subjects        |                        |                   |                        |
| Adults (18-64 years)   |                        |                   |                        |
| From 65-84 years       |                        |                   |                        |
| 85 years and over      |                        |                   |                        |
| Age Continuous         |                        |                   |                        |
| "999"=N/A              |                        |                   |                        |
| Units: years           |                        |                   |                        |
| arithmetic mean        |                        |                   |                        |
| standard deviation     | ±                      | ±                 | ±                      |

|   |  |  |  |
|---|--|--|--|
| Sex: Female, Male<br>Units:   |  |  |  |
| Female  |  |  |  |
| Male  |  |  |  |
| Race (NIH/OMB)<br>Units: Subjects   |  |  |  |
| American Indian or Alaska Native<br>Asian<br>Native Hawaiian or Other Pacific Islander<br>Black or African American<br>White<br>More than one race<br>Unknown or Not Reported |  |  |  |
| Ethnicity (NIH/OMB)<br>Units: Subjects  |  |  |  |
| Hispanic or Latino<br>Not Hispanic or Latino<br>Unknown or Not Reported   |  |  |  |

| <b>Reporting group values</b>   | N3 30M BM, W2 | N3 60M, W4 | N3 30M, W2 |
|---|---------------|------------|------------|
| Number of subjects  | 3             | 75         | 12         |
| Age categorical<br>Units: Subjects  |               |            |            |
| Adults (18-64 years)<br>From 65-84 years<br>85 years and over   |               |            |            |
| Age Continuous  |               |            |            |
| "999"=N/A   |               |            |            |
| Units: years<br>arithmetic mean<br>standard deviation   | ±             | ±          | ±          |
| Sex: Female, Male<br>Units:   |               |            |            |
| Female  |               |            |            |
| Male  |               |            |            |
| Race (NIH/OMB)<br>Units: Subjects   |               |            |            |
| American Indian or Alaska Native<br>Asian<br>Native Hawaiian or Other Pacific Islander<br>Black or African American<br>White<br>More than one race<br>Unknown or Not Reported |               |            |            |
| Ethnicity (NIH/OMB)<br>Units: Subjects  |               |            |            |
| Hispanic or Latino<br>Not Hispanic or Latino<br>Unknown or Not Reported   |               |            |            |

| Reporting group values  | N1 + I3, W2 | N1 + I3 W2, NON-BM | N3 NAIVE, NON-BM |
|---|-------------|--------------------|------------------|
| Number of subjects  | 37          | 33                 | 48               |
| Age categorical<br>Units: Subjects  |             |                    |                  |
| Adults (18-64 years)<br>From 65-84 years<br>85 years and over   |             |                    |                  |
| Age Continuous  |             |                    |                  |
| "999"=N/A   |             |                    |                  |
| Units: years<br>arithmetic mean<br>standard deviation   | ±           | ±                  | ±                |
| Sex: Female, Male<br>Units:   |             |                    |                  |
| Female<br>Male  |             |                    |                  |
| Race (NIH/OMB)<br>Units: Subjects   |             |                    |                  |
| American Indian or Alaska Native<br>Asian<br>Native Hawaiian or Other Pacific Islander<br>Black or African American<br>White<br>More than one race<br>Unknown or Not Reported |             |                    |                  |
| Ethnicity (NIH/OMB)<br>Units: Subjects  |             |                    |                  |
| Hispanic or Latino<br>Not Hispanic or Latino<br>Unknown or Not Reported   |             |                    |                  |

| Reporting group values  | N1 + I3 NON-BM | Total | N1 + I3 NON-BM |
|---|----------------|-------|----------------|
| Number of subjects  | 49             | 140   | 52             |
| Age categorical<br>Units: Subjects                            |                |       |                |
| Adults (18-64 years)<br>From 65-84 years<br>85 years and over |                |       |                |
| Age Continuous  |                |       |                |
| "999"=N/A   |                |       |                |
| Units: years<br>arithmetic mean<br>standard deviation         | ±              | ±     | ±              |
| Sex: Female, Male<br>Units:                                   |                |       |                |
| Female<br>Male  |                |       |                |
| Race (NIH/OMB)<br>Units: Subjects                             |                |       |                |
| American Indian or Alaska Native                              |                |       |                |

|   |  |  |  |
|---|--|--|--|
| Asian<br>Native Hawaiian or Other Pacific Islander<br>Black or African American<br>White<br>More than one race<br>Unknown or Not Reported |  |  |  |
| Ethnicity (NIH/OMB)<br>Units: Subjects  |  |  |  |
| Hispanic or Latino<br>Not Hispanic or Latino<br>Unknown or Not Reported   |  |  |  |

| Reporting group values  | N3 NAIVE | All N3 | N1 + I3 |
|---|----------|--------|---------|
| Number of subjects  | 62       | 106    | 62      |
| Age categorical<br>Units: Subjects  |          |        |         |
| Adults (18-64 years)<br>From 65-84 years<br>85 years and over   |          |        |         |
| Age Continuous  |          |        |         |
| "999"=N/A   |          |        |         |
| Units: years<br>arithmetic mean<br>standard deviation   | ±        | ±      | ±       |
| Sex: Female, Male<br>Units:   |          |        |         |
| Female<br>Male  |          |        |         |
| Race (NIH/OMB)<br>Units: Subjects   |          |        |         |
| American Indian or Alaska Native<br>Asian<br>Native Hawaiian or Other Pacific Islander<br>Black or African American<br>White<br>More than one race<br>Unknown or Not Reported |          |        |         |
| Ethnicity (NIH/OMB)<br>Units: Subjects  |          |        |         |
| Hispanic or Latino<br>Not Hispanic or Latino<br>Unknown or Not Reported   |          |        |         |

| Reporting group values  | Total |  |  |
|---|-------|--|--|
| Number of subjects  | 168   |  |  |
| Age categorical<br>Units: Subjects                            |       |  |  |
| Adults (18-64 years)<br>From 65-84 years<br>85 years and over |       |  |  |



|   |       |  |  |
|---|-------|--|--|
| Age Continuous  |       |  |  |
| "999"=N/A   |       |  |  |
| Units: years<br>arithmetic mean<br>standard deviation   | $\pm$ |  |  |
| Sex: Female, Male   |       |  |  |
| Units:  |       |  |  |
| Female<br>Male  |       |  |  |
| Race (NIH/OMB)  |       |  |  |
| Units: Subjects   |       |  |  |
| American Indian or Alaska Native<br>Asian<br>Native Hawaiian or Other Pacific Islander<br>Black or African American<br>White<br>More than one race<br>Unknown or Not Reported |       |  |  |
| Ethnicity (NIH/OMB)   |       |  |  |
| Units: Subjects   |       |  |  |
| Hispanic or Latino<br>Not Hispanic or Latino<br>Unknown or Not Reported   |       |  |  |

## End points

### End points reporting groups

|   |                        |
|---|------------------------|
| Reporting group title   | N3 60 M Naive          |
| Reporting group description:  |                        |
| Treatment Group: N3 = Nivolumab 3mg/kg; 60M = 60 minute infusion; Naive = Anti-CTLA4 Naive  |                        |
| Reporting group title   | N3 60M Prog            |
| Reporting group description:  |                        |
| Treatment Group: N3 = Nivolumab 3mg/kg; 60M = 60 minute infusion; PROG = Anti-CTLA4 Progressed  |                        |
| Reporting group title   | N1 60M + I3 90M, W2    |
| Reporting group description:  |                        |
| Treatment Group: N1 = Nivolumab 1mg/kg; I3 = Ipilimumab 3 mg/kg; 90M = 90 minute infusion; 60M = 60 minute infusion; W2 = Week 2 Biopsy       |                        |
| Reporting group title   | N1 60M + I3 90M, W4    |
| Reporting group description:  |                        |
| Treatment Group: N1 = Nivolumab 1mg/kg; I3 = Ipilimumab 3 mg/kg; 90M = 90 minute infusion; 60M = 60 minute infusion; W4 = Week 4 Biopsy       |                        |
| Reporting group title   | N1 60M +I3 90M, WU     |
| Reporting group description:  |                        |
| Treatment Group: N1 = Nivolumab 1mg/kg; I3 = Ipilimumab 3 mg/kg; 90M = 90 minute infusion; 60M = 60 minute infusion; WU = Unknown Week Biopsy |                        |
| Reporting group title   | N1 30M + I3 30M non-BM |
| Reporting group description:  |                        |
| Treatment Group: N1 = Nivolumab 1mg/kg; I3 = Ipilimumab 3 mg/kg; 30M = 30 minute infusion; BM = Brain metastases                              |                        |
| Reporting group title   | N3 30M non-BM          |
| Reporting group description:  |                        |
| Treatment Group: N3 = Nivolumab 3mg/kg;30M = 30 minute infusion; BM = Brain metastases  |                        |
| Reporting group title   | N1 30M +I3 30M BM      |
| Reporting group description:  |                        |
| Treatment Group: N1 = Nivolumab 1mg/kg; I3 = Ipilimumab 3 mg/kg; 30M = 30 minute infusion; BM = Brain metastases                              |                        |
| Reporting group title   | N3 30M BM              |
| Reporting group description:  |                        |
| Treatment Group: N3 = Nivolumab 3mg/kg; 30M = 30 minute infusion; BM = Brain metastases   |                        |
| Reporting group title   | I3 Monotherapy         |
| Reporting group description:  |                        |
| Treatment Group: I3 = Ipilimumab 3 mg/kg infusion. Participant was enrolled prior to the closure of this arm via amendment                    |                        |
| Reporting group title   | Unplanned Treatment    |
| Reporting group description:  |                        |
| Unplanned treatment of nivolumab 1 mg/kg x 4 then nivolumab 3 mg/kg   |                        |
| Subject analysis set title  | N3 60M Naive           |
| Subject analysis set type   | Sub-group analysis     |
| Subject analysis set description:   |                        |
| Treatment Group: Part 1: Nivolumab 3 mg/kg 60 Minute Infusion Anti-CTLA4 Naive  |                        |
| Subject analysis set title  | N3 60M PROG            |
| Subject analysis set type   | Sub-group analysis     |
| Subject analysis set description:   |                        |
| Treatment Group: N3 = Nivolumab 3mg/kg; 60M = 60 minute infusion; PROG = Anti-CTLA4 Progressed  |                        |
| Subject analysis set title  | N1 60M + I3 90M        |
| Subject analysis set type   | Sub-group analysis     |

Subject analysis set description:

Treatment Group: Part 2: Nivolumab 1 mg/kg 60 Minute Infusion + Ipilimumab 3 mg/kg 90 Minute

|                            |                    |
|----------------------------|--------------------|
| Subject analysis set title | N1 30M + I3 30M BM |
| Subject analysis set type  | Sub-group analysis |

Subject analysis set description:

Treatment Group: N1 = Nivolumab 1mg/kg; I3 = Ipilimumab 3 mg/kg; 30M = 30 minute infusion; BM = Brain metastases

|                            |                    |
|----------------------------|--------------------|
| Subject analysis set title | N1+ I3 Non-BM      |
| Subject analysis set type  | Sub-group analysis |

Subject analysis set description:

Treatment Group: Part 2+3: Nivolumab 1 mg/kg + Ipilimumab 3 mg/kg Non-Brain Metastases

|                            |                    |
|----------------------------|--------------------|
| Subject analysis set title | Naive Nivo Mono    |
| Subject analysis set type  | Sub-group analysis |

Subject analysis set description:

Nivolumab Monotherapy CTLA-4 Naive

|                            |                    |
|----------------------------|--------------------|
| Subject analysis set title | All Nivo           |
| Subject analysis set type  | Sub-group analysis |

Subject analysis set description:

Treatment Group: All Nivolumab Monotherapy

|                            |                    |
|----------------------------|--------------------|
| Subject analysis set title | All Combo          |
| Subject analysis set type  | Sub-group analysis |

Subject analysis set description:

Treatment Group: All Combination Therapy

|                            |                    |
|----------------------------|--------------------|
| Subject analysis set title | Total              |
| Subject analysis set type  | Sub-group analysis |

Subject analysis set description:

All treatments

|                            |                    |
|----------------------------|--------------------|
| Subject analysis set title | N3 60M Naive       |
| Subject analysis set type  | Sub-group analysis |

Subject analysis set description:

Treatment Group: Part 1: Nivolumab 3 mg/kg 60 Minute Infusion Anti-CTLA4 Naive

|                            |                    |
|----------------------------|--------------------|
| Subject analysis set title | N3 60M PROG        |
| Subject analysis set type  | Sub-group analysis |

Subject analysis set description:

Treatment Group: N3 = Nivolumab 3mg/kg; 60M = 60 minute infusion; PROG = Anti-CTLA4 Progressed

|                            |                    |
|----------------------------|--------------------|
| Subject analysis set title | N1 60M + I3 90M W2 |
| Subject analysis set type  | Sub-group analysis |

Subject analysis set description:

Treatment Group: Part 2: Nivolumab 1 mg/kg 60 Minute Infusion + Ipilimumab 3 mg/kg 90 Minute Infusion Week 2 Biopsy

|                            |                    |
|----------------------------|--------------------|
| Subject analysis set title | N1 60M + I3 90M W4 |
| Subject analysis set type  | Sub-group analysis |

Subject analysis set description:

Treatment Group: Part 2: Nivolumab 1 mg/kg 60 Minute Infusion + Ipilimumab 3 mg/kg 90 Minute Infusion Week 4 Biopsy

|                            |                    |
|----------------------------|--------------------|
| Subject analysis set title | N3 30M + I3 30M BM |
| Subject analysis set type  | Sub-group analysis |

Subject analysis set description:

Treatment Group: Part 4: Nivolumab 1 mg/kg 30 Minute Infusion + Ipilimumab 3 mg/kg 30 Minute Infusion Brain Metastases

|                            |                    |
|----------------------------|--------------------|
| Subject analysis set title | Nivo Mono          |
| Subject analysis set type  | Sub-group analysis |

Subject analysis set description:

Treatment Group: Part 1: Regular Infusion Nivolumab Mono

|                            |                            |
|----------------------------|----------------------------|
| Subject analysis set title | Nivo Mono Reduced Infusion |
| Subject analysis set type  | Sub-group analysis         |

Subject analysis set description:

Treatment Group: Reduced Infusion Nivolumab Monotherapy

|                            |                     |
|----------------------------|---------------------|
| Subject analysis set title | Week 2 Biopsy Combo |
| Subject analysis set type  | Sub-group analysis  |

Subject analysis set description:

Treatment Group: Week 2 Biopsy Combo

|                            |                            |
|----------------------------|----------------------------|
| Subject analysis set title | Week 2 Biopsy non-BM Combo |
| Subject analysis set type  | Sub-group analysis         |

Subject analysis set description:

Treatment Group: Week 2 Biopsy Non-Brain Metastases Combo

|                            |                        |
|----------------------------|------------------------|
| Subject analysis set title | Naive Nivo Mono non-BM |
| Subject analysis set type  | Sub-group analysis     |

Subject analysis set description:

Treatment Group: Naive Nivolumab Mono Non-Brain Metastases

|                            |                    |
|----------------------------|--------------------|
| Subject analysis set title | N1 + I3 non-BM     |
| Subject analysis set type  | Sub-group analysis |

Subject analysis set description:

Treatment Group: Part 2+3: Nivolumab 1 mg/kg + Ipilimumab 3 mg/kg Non-Brain Metastases

|                            |                    |
|----------------------------|--------------------|
| Subject analysis set title | N3 60M Naive       |
| Subject analysis set type  | Sub-group analysis |

Subject analysis set description:

N3 = Nivolumab 3mg/kg; 60M = 60 minute infusion; NAIVE = Anti-CTLA4 Naive

|                            |                    |
|----------------------------|--------------------|
| Subject analysis set title | N3 60M PROG        |
| Subject analysis set type  | Sub-group analysis |

Subject analysis set description:

Treatment Group: N3 = Nivolumab 3mg/kg; 60M = 60 minute infusion; PROG = Anti-CTLA4 Progressed

|                            |                    |
|----------------------------|--------------------|
| Subject analysis set title | N1 60M + I3 90M    |
| Subject analysis set type  | Sub-group analysis |

Subject analysis set description:

N1 = Nivolumab 1mg/kg; I3 = Ipilimumab 3 mg/kg; 90M = 90 minute infusion; 60M = 60 minute infusion

|                            |                    |
|----------------------------|--------------------|
| Subject analysis set title | N1 30M + I3 30M BM |
| Subject analysis set type  | Sub-group analysis |

Subject analysis set description:

Treatment Group: N1 = Nivolumab 1mg/kg; I3 = Ipilimumab 3 mg/kg; 30M = 30 minute infusion; BM = Brain metastases

|                            |                    |
|----------------------------|--------------------|
| Subject analysis set title | N3 60M Naive       |
| Subject analysis set type  | Sub-group analysis |

Subject analysis set description:

Part 1: Nivolumab 3 mg/kg 60 Minute Infusion Anti-CTLA4 Naive

|                            |                    |
|----------------------------|--------------------|
| Subject analysis set title | N1 60M + I3 90M    |
| Subject analysis set type  | Sub-group analysis |

Subject analysis set description:

Part 2: Nivolumab 1 mg/kg 60 Minute Infusion + Ipilimumab 3 mg/kg 90 Minute Infusion

|                            |                        |
|----------------------------|------------------------|
| Subject analysis set title | N1 30M + I3 30M Non-BM |
| Subject analysis set type  | Sub-group analysis     |

Subject analysis set description:

Part 3: Nivolumab 1 mg/kg 30 Minute Infusion + Ipilimumab 3 mg/kg 30 Minute Infusion Non-Brain Metastases

|   |                        |
|---|------------------------|
| Subject analysis set title  | N3 30M Non-BM          |
| Subject analysis set type   | Sub-group analysis     |
| Subject analysis set description:   |                        |
| Part 3: Nivolumab 3 mg/kg 30 Minute Infusion Non-Brain Metastases   |                        |
| Subject analysis set title  | N1 30M I3 30M BM       |
| Subject analysis set type   | Sub-group analysis     |
| Subject analysis set description:   |                        |
| Part 4: Nivolumab 1 mg/kg 30 Minute Infusion + Ipilimumab 3 mg/kg 30 Minute Infusion Brain Metastases               |                        |
| Subject analysis set title  | N3 60M NAIVE           |
| Subject analysis set type   | Sub-group analysis     |
| Subject analysis set description:   |                        |
| Treatment Group: N3 = Nivolumab 3mg/kg; 60M = 60 minute infusion; Naive = Anti-CTLA4 Naive                          |                        |
| Subject analysis set title  | N1 60M +I3 90M         |
| Subject analysis set type   | Sub-group analysis     |
| Subject analysis set description:   |                        |
| Treatment Group: N1 = Nivolumab 1mg/kg; I3 = Ipilimumab 3 mg/kg; 90M = 90 minute infusion; 60M = 60 minute infusion |                        |
| Subject analysis set title  | N3 60M NAIVE           |
| Subject analysis set type   | Sub-group analysis     |
| Subject analysis set description:   |                        |
| Treatment Group: N3 = Nivolumab 3mg/kg; 60M = 60 minute infusion; Naive = Anti-CTLA4 Naive                          |                        |
| Subject analysis set title  | N3 60M PROG            |
| Subject analysis set type   | Sub-group analysis     |
| Subject analysis set description:   |                        |
| Treatment Group: N3 = Nivolumab 3mg/kg; 60M = 60 minute infusion; PROG = Anti-CTLA4 Progressed                      |                        |
| Subject analysis set title  | N1 60M +I3 90M         |
| Subject analysis set type   | Sub-group analysis     |
| Subject analysis set description:   |                        |
| Treatment Group: N1 = Nivolumab 1mg/kg; I3 = Ipilimumab 3 mg/kg; 90M = 90 minute infusion; 60M = 60 minute infusion |                        |
| Subject analysis set title  | N1 60M+I3 90M          |
| Subject analysis set type   | Sub-group analysis     |
| Subject analysis set description:   |                        |
| N1 = Nivolumab 1mg/kg; I3 = Ipilimumab 3 mg/kg; 90M = 90 minute infusion; 60M = 60 minute infusion                  |                        |
| Subject analysis set title  | N1 30M + I3 30M BM     |
| Subject analysis set type   | Sub-group analysis     |
| Subject analysis set description:   |                        |
| N3 = Nivolumab 3mg/kg; I3 = Ipilimumab 3 mg/kg; 30M = 30 minute infusion; BM = Brain metastases                     |                        |
| Subject analysis set title  | N1 30M + I3 30M NON-BM |
| Subject analysis set type   | Sub-group analysis     |
| Subject analysis set description:   |                        |
| N1 = Nivolumab 1mg/kg; I3 = Ipilimumab 3 mg/kg; 30M = 30 minute infusion; BM = Brain metastases                     |                        |
| Subject analysis set title  | N3 30M NON-BM          |
| Subject analysis set type   | Sub-group analysis     |
| Subject analysis set description:   |                        |
| N3 = Nivolumab 3mg/kg; 30M = 30 minute infusion; BM = Brain metastases  |                        |
| Subject analysis set title  | N3 60M NAIVE           |
| Subject analysis set type   | Sub-group analysis     |
| Subject analysis set description:   |                        |
| Treatment Group: N3 = Nivolumab 3mg/kg; 60M = 60 minute infusion; Naive = Anti-CTLA4 Naive                          |                        |
| Subject analysis set title  | N3 60M PROG            |

|   |                                   |
|---|-----------------------------------|
| Subject analysis set type   | Sub-group analysis                |
| Subject analysis set description:   |                                   |
| Treatment Group: N3 = Nivolumab 3mg/kg; 60M = 60 minute infusion; PROG = Anti-CTLA4 Progressed  |                                   |
| Subject analysis set title  | N1 60M + I3 (Nivo ADA)            |
| Subject analysis set type   | Sub-group analysis                |
| Subject analysis set description:   |                                   |
| Part 2: Nivolumab 1 mg/kg 60 Minute Infusion + Ipilimumab 3 mg/kg 90 Minute   |                                   |
| Subject analysis set title  | N1 60M + I3 90M (Ipi ADA)         |
| Subject analysis set type   | Sub-group analysis                |
| Subject analysis set description:   |                                   |
| Part 2: Nivolumab 1 mg/kg 60 Minute Infusion + Ipilimumab 3 mg/kg 90 Minute   |                                   |
| Subject analysis set title  | N1 30M + I3 30M Non-BM (Nivo ADA) |
| Subject analysis set type   | Sub-group analysis                |
| Subject analysis set description:   |                                   |
| Part 3: Nivolumab 1 mg/kg 30 Minute Infusion + Ipilimumab 3 mg/kg 30 Minute Infusion Non-Brain Metastases                                     |                                   |
| Subject analysis set title  | N1 30M + I3 30M Non-BM (Ipi ADA)  |
| Subject analysis set type   | Sub-group analysis                |
| Subject analysis set description:   |                                   |
| Part 3: Nivolumab 1 mg/kg 30 Minute Infusion + Ipilimumab 3 mg/kg 30 Minute Infusion Non-Brain Metastases                                     |                                   |
| Subject analysis set title  | N1 30M + I3 30M (Nivo ADA)        |
| Subject analysis set type   | Sub-group analysis                |
| Subject analysis set description:   |                                   |
| Part 4: Nivolumab 1 mg/kg 30 Minute Infusion + Ipilimumab 3 mg/kg 30 Minute Infusion Brain Metastases   |                                   |
| Subject analysis set title  | N1 30M + I3 30M (Ipi ADA)         |
| Subject analysis set type   | Sub-group analysis                |
| Subject analysis set description:   |                                   |
| Part 4: Nivolumab 1 mg/kg 30 Minute Infusion + Ipilimumab 3 mg/kg 30 Minute Infusion Brain Metastases   |                                   |
| Subject analysis set title  | Total (Nivo ADA)                  |
| Subject analysis set type   | Sub-group analysis                |
| Subject analysis set description:   |                                   |
| Total (All Nivolumab or Nivolumab + Ipilimumab Treated Subjects with Baseline and at Least One Post-Baseline Assessment)                      |                                   |
| Subject analysis set title  | Total (Ipi ADA)                   |
| Subject analysis set type   | Sub-group analysis                |
| Subject analysis set description:   |                                   |
| Total (All Nivolumab or Nivolumab + Ipilimumab Treated Subjects with Baseline and at Least One Post-Baseline Assessment)                      |                                   |
| Subject analysis set title  | N3 60M NAIVE, W4                  |
| Subject analysis set type   | Sub-group analysis                |
| Subject analysis set description:   |                                   |
| Treatment Group: N3 = Nivolumab 3mg/kg; 60M = 60 minute infusion; NAIVE = Anti-CTLA4 Naive  |                                   |
| Subject analysis set title  | N3 60M PROG, W4                   |
| Subject analysis set type   | Sub-group analysis                |
| Subject analysis set description:   |                                   |
| Treatment Group: N3 = Nivolumab 3mg/kg; 60M = 60 minute infusion; PROG = Anti-CTLA4 Progressed;   |                                   |
| Subject analysis set title  | N1 60M + I3 90M, WU               |
| Subject analysis set type   | Sub-group analysis                |
| Subject analysis set description:   |                                   |
| Treatment Group: N1 = Nivolumab 1mg/kg; I3 = Ipilimumab 3 mg/kg; 90M = 90 minute infusion; 60M = 60 minute infusion; WU = Unknown Week Biopsy |                                   |

|  |                        |
|--|------------------------|
| Subject analysis set title   | N1 30M + I3 30M NON-BM |
| Subject analysis set type  | Sub-group analysis     |
| Subject analysis set description:  |                        |
| Treatment Group: N1 = Nivolumab 1mg/kg; I3 = Ipilimumab 3 mg/kg; 30M = 30 minute infusion; BM = Brain metastases |                        |
| Subject analysis set title   | N3 30M NON-BM, W2      |
| Subject analysis set type  | Sub-group analysis     |
| Subject analysis set description:  |                        |
| Treatment Group: N3 = Nivolumab 3mg/kg; 30M = 30 minute infusion; W2 = Week 2 Biopsy                             |                        |
| Subject analysis set title   | N1 30M + I3 30M BM, W2 |
| Subject analysis set type  | Sub-group analysis     |
| Subject analysis set description:  |                        |
| Treatment Group: N1 = Nivolumab 1mg/kg; I3 = Ipilimumab 3 mg/kg; 30M = 30 minute infusion; W2 = Week 2 Biopsy    |                        |
| Subject analysis set title   | N3 30M BM, W2          |
| Subject analysis set type  | Sub-group analysis     |
| Subject analysis set description:  |                        |
| Treatment Group: N3 = Nivolumab 3mg/kg; 30M = 30 minute infusion; W2 = Week 2 Biopsy                             |                        |
| Subject analysis set title   | N3 60M, W4             |
| Subject analysis set type  | Sub-group analysis     |
| Subject analysis set description:  |                        |
| N3 = Nivolumab 3mg/kg; 60M = 60 minute infusion; W4 = Week 4 Biopsy  |                        |
| Subject analysis set title   | N3 30M, W2             |
| Subject analysis set type  | Sub-group analysis     |
| Subject analysis set description:  |                        |
| Treatment Group: N3 = Nivolumab 3mg/kg; 30M = 30 minute infusion; W2 = Week 2 Biopsy                             |                        |
| Subject analysis set title   | N1 + I3, W2            |
| Subject analysis set type  | Sub-group analysis     |
| Subject analysis set description:  |                        |
| N1 = Nivolumab 1mg/kg; I3 = Ipilimumab 3 mg/kg; W2 = Week 2 Biopsy   |                        |
| Subject analysis set title   | N1 + I3 W2, NON-BM     |
| Subject analysis set type  | Sub-group analysis     |
| Subject analysis set description:  |                        |
| N1 = Nivolumab 1mg/kg; I3 = Ipilimumab 3 mg/kg; W2 = Week 2 Biopsy; BM = Brain metastases                        |                        |
| Subject analysis set title   | N3 NAIVE, NON-BM       |
| Subject analysis set type  | Sub-group analysis     |
| Subject analysis set description:  |                        |
| N3 = Nivolumab 3mg/kg; NAIVE = Anti-CTLA4 Naive; BM = Brain metastases   |                        |
| Subject analysis set title   | N1 + I3 NON-BM         |
| Subject analysis set type  | Sub-group analysis     |
| Subject analysis set description:  |                        |
| N1 = Nivolumab 1mg/kg; I3 = Ipilimumab 3 mg/kg; BM = Brain metastases  |                        |
| Subject analysis set title   | Total                  |
| Subject analysis set type  | Sub-group analysis     |
| Subject analysis set description:  |                        |
| All treatments   |                        |
| Subject analysis set title   | N1 + I3 NON-BM         |
| Subject analysis set type  | Sub-group analysis     |
| Subject analysis set description:  |                        |
| N1 = Nivolumab 1mg/kg; I3 = Ipilimumab 3 mg/kg; BM = Brain metastases  |                        |
| Subject analysis set title   | N3 NAIVE               |
| Subject analysis set type  | Sub-group analysis     |

Subject analysis set description:

N3 = Nivolumab 3mg/kg; NAIVE = Anti-CTLA4 Naive

|                            |                    |
|----------------------------|--------------------|
| Subject analysis set title | All N3             |
| Subject analysis set type  | Sub-group analysis |

Subject analysis set description:

N3 = Nivolumab 3mg/kg

|                            |                    |
|----------------------------|--------------------|
| Subject analysis set title | N1 + I3            |
| Subject analysis set type  | Sub-group analysis |

Subject analysis set description:

All combination

|                            |                    |
|----------------------------|--------------------|
| Subject analysis set title | Total              |
| Subject analysis set type  | Sub-group analysis |

Subject analysis set description:

All treatments

### Primary: Median change from baseline to week 7, of Interferon (IFN) and interferon gamma (IFN-gamma) inducible factors

|                 |   |
|-----------------|---|
| End point title | Median change from baseline to week 7, of Interferon (IFN) and interferon gamma (IFN-gamma) inducible factors <sup>[1][2]</sup> |
|-----------------|---|

End point description:

Baseline and post-treatment modulation of serum levels of chemokines, cytokines and other immune mediators were assessed by techniques that included ELISA or other multiplex-based assay methods. Primary analysis included IFN-gamma and IFN-gamma inducible factors, including chemokine [C-X-C motif] ligand 9 (CXCL9) and CXCL10

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

End point timeframe:

From last non-missing value prior to first dose to week 7 day 1

Notes:

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

Justification: All participants listed in the baseline period who received treatment per the protocol are reported in the subject analysis sets which are subsets of the full population.

[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.

Justification: All participants listed in the baseline period who received treatment per the protocol are reported in the subject analysis sets which are subsets of the full population.

| End point values            | N1 30M + I3<br>30M non-BM | N3 30M non-<br>BM    | N3 30M BM            | N3 60M Naive          |
|-----------------------------|---------------------------|----------------------|----------------------|-----------------------|
| Subject group type          | Reporting group           | Reporting group      | Reporting group      | Subject analysis set  |
| Number of subjects analysed | 23                        | 11                   | 7                    | 40                    |
| Units: pg/mL                |                           |                      |                      |                       |
| median (standard deviation) |                           |                      |                      |                       |
| IFN-gamma Simoa             | 0.1600 (±<br>1.2047)      | 0.0520 (±<br>0.1207) | 0.0375 (±<br>0.1868) | 0.0130 (±<br>0.1740)  |
| CXL9 (aka MIG)              | 3542.0 (±<br>12133.1)     | -29.0 (±<br>1684.2)  | 3610.0 (±<br>2197.4) | 1105.0 (±<br>10467.4) |
| CXL10 (aka IP10)            | 934.5 (±<br>2842.0)       | 26.0 (± 172.7)       | 318.0 (±<br>354.0)   | 184.0 (±<br>514.1)    |

| End point values            | N3 60M PROG          | N1 60M + I3<br>90M   | N1 30M + I3<br>30M BM | N1+ I3 Non-<br>BM    |
|-----------------------------|----------------------|----------------------|-----------------------|----------------------|
| Subject group type          | Subject analysis set | Subject analysis set | Subject analysis set  | Subject analysis set |
| Number of subjects analysed | 40                   | 27                   | 8                     | 50                   |



|                             |                   |                    |                   |                   |
|-----------------------------|-------------------|--------------------|-------------------|-------------------|
| Units: pg/mL                |                   |                    |                   |                   |
| median (standard deviation) |                   |                    |                   |                   |
| IFN-gamma Simoa             | 0.0320 (± 0.0817) | 0.2310 (± 0.4528)  | 0.0950 (± 1.5082) | 0.2200 (± 0.8198) |
| CXL9 (aka MIG)              | 1890.0 (± 8706.0) | 4680.0 (± 18096.9) | 5692.0 (± 6796.0) | 458.5 (± 1651.0)  |
| CXL10 (aka IP10)            | 160.0 (± 539.9)   | 684.0 (± 2563.1)   | 514.0 (± 612.3)   | 695.0 (± 2627.7)  |

| End point values            | Naive Nivo Mono      | All Nivo             | All Combo            | Total                |
|-----------------------------|----------------------|----------------------|----------------------|----------------------|
| Subject group type          | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 58                   | 98                   | 58                   | 156                  |
| Units: pg/mL                |                      |                      |                      |                      |
| median (standard deviation) |                      |                      |                      |                      |
| IFN-gamma Simoa             | 0.0130 (± 0.1674)    | 0.0240 (± 0.1373)    | 0.1520 (± 1.0023)    | 0.0515 (± 0.5944)    |
| CXL9 (aka MIG)              | 1056.5 (± 9167.8)    | 1235.0 (± 8984.2)    | 4680.0 (± 14792.5)   | 2027.0 (± 11491.9)   |
| CXL10 (aka IP10)            | 185.0 (± 474.6)      | 184.0 (± 500.7)      | 684.0 (± 2450.6)     | 234.5 (± 1566.3)     |

## Statistical analyses

No statistical analyses for this end point

## Primary: Tumor infiltrating lymphocytes (TILs) as measured by medians in percent positive CD8 and positive CD4 at baseline and on-treatment biopsy, both using the Mosaic Singleplex IHC assay

|                 |   |
|-----------------|---|
| End point title | Tumor infiltrating lymphocytes (TILs) as measured by medians in percent positive CD8 and positive CD4 at baseline and on-treatment biopsy, both using the Mosaic Singleplex IHC assay <sup>[3][4]</sup> |
|-----------------|---|

End point description:

Biomarkers examined were percent positive CD8 and percent positive CD4, both using the Mosaic Singleplex IHC assay. Analyses are presented with the medians at baseline and on-treatment, rather than the median change because the baseline values differed across groups. Baseline was defined as the last non-missing value on or prior to the first dose of study therapy. Biopsies were also collected on treatment.

"999"=N/A

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

End point timeframe:

From last non-missing value prior to first dose to week 4 day 1

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: All participants listed in the baseline period who received treatment per the protocol are reported in the subject analysis sets which are subsets of the full population.

[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: All participants listed in the baseline period who received treatment per the protocol are reported in the subject analysis sets which are subsets of the full population.

| End point values                    | N1 30M + I3<br>30M non-BM | N3 30M non-<br>BM | N3 30M BM        | N3 60M Naive         |
|-------------------------------------|---------------------------|-------------------|------------------|----------------------|
| Subject group type                  | Reporting group           | Reporting group   | Reporting group  | Subject analysis set |
| Number of subjects analysed         | 15                        | 10                | 2                | 25                   |
| Units: Percentage of positive cells |                           |                   |                  |                      |
| median (standard deviation)         |                           |                   |                  |                      |
| Percent CD8 Baseline                | 4.700 (± 9.810)           | 5.615 (± 12.475)  | 6.135 (± 5.664)  | 3.73 (± 10.994)      |
| Percent positive CD8 Week 2         | 7.970 (± 15.132)          | 10.100 (± 10.909) | 29.735 (± 5.254) | 999 (± 999)          |
| Percent positive CD8 Week 4         | 37.465 (± 5.706)          | 999 (± 999)       | 999 (± 999)      | 18.435 (± 17.108)    |
| Percent CD4 Baseline                | 4.155 (± 6.624)           | 4.950 (± 4.992)   | 2.780 (± 999)    | 0.360 (± 1.844)      |
| Percent positive CD4 Week 2         | 6.260 (± 8.518)           | 4.210 (± 5.029)   | 20.830 (± 999)   | 999 (± 999)          |
| Percent positive CD4 Week 4         | 24.520 (± 2.659)          | 999 (± 999)       | 999 (± 999)      | 1.585 (± 3.071)      |

| End point values                    | N3 60M PROG          | N1 60M + I3<br>90M W2 | N1 60M + I3<br>90M W4 | N3 30M + I3<br>30M BM |
|-------------------------------------|----------------------|-----------------------|-----------------------|-----------------------|
| Subject group type                  | Subject analysis set | Subject analysis set  | Subject analysis set  | Subject analysis set  |
| Number of subjects analysed         | 23                   | 11                    | 10                    | 3                     |
| Units: Percentage of positive cells |                      |                       |                       |                       |
| median (standard deviation)         |                      |                       |                       |                       |
| Percent CD8 Baseline                | 7.230 (± 10.712)     | 3.260 (± 9.259)       | 11.105 (± 9.524)      | 18.590 (± 8.132)      |
| Percent positive CD8 Week 2         | 999 (± 999)          | 11.345 (± 21.316)     | 999 (± 999)           | 8.470 (± 7.740)       |
| Percent positive CD8 Week 4         | 7.140 (± 25.204)     | 999 (± 999)           | 32.455 (± 15.967)     | 999 (± 999)           |
| Percent CD4 Baseline                | 0.600 (± 2.268)      | 0.840 (± 1.852)       | 0.470 (± 3.833)       | 6.500 (± 8.108)       |
| Percent positive CD4 Week 2         | 999 (± 999)          | 4.500 (± 10.741)      | 999 (± 999)           | 6.420 (± 14.778)      |
| Percent positive CD4 Week 4         | 1.260 (± 4.641)      | 999 (± 999)           | 9.005 (± 13.324)      | 999 (± 999)           |

| End point values                    | Nivo Mono            | Nivo Mono<br>Reduced<br>Infusion | Week 2 Biopsy<br>Combo | Week 2 Biopsy<br>non-BM Combo |
|-------------------------------------|----------------------|----------------------------------|------------------------|-------------------------------|
| Subject group type                  | Subject analysis set | Subject analysis set             | Subject analysis set   | Subject analysis set          |
| Number of subjects analysed         | 48                   | 12                               | 29                     | 26                            |
| Units: Percentage of positive cells |                      |                                  |                        |                               |
| median (standard deviation)         |                      |                                  |                        |                               |
| Percent CD8 Baseline                | 6.360 (± 10.727)     | 5.615 (± 11.472)                 | 4.700 (± 9.292)        | 4.230 (± 9.401)               |
| Percent positive CD8 Week 2         | 999 (± 999)          | 10.910 (± 12.387)                | 9.080 (± 17.510)       | 9.125 (± 18.654)              |
| Percent positive CD8 Week 4         | 15.150 (± 21.475)    | 999 (± 999)                      | 37.465 (± 5.706)       | 37.465 (± 5.706)              |
| Percent CD4 Baseline                | 0.375 (± 2.057)      | 4.600 (± 4.807)                  | 2.750 (± 5.833)        | 2.610 (± 5.607)               |

|                             |                 |                 |                  |                  |
|-----------------------------|-----------------|-----------------|------------------|------------------|
| Percent positive CD4 Week 2 | 999 (± 999)     | 6.155 (± 6.585) | 6.125 (± 10.222) | 5.990 (± 9.602)  |
| Percent positive CD4 Week 4 | 1.275 (± 3.921) | 999 (± 999)     | 24.520 (± 2.659) | 24.520 (± 2.659) |

| End point values                    | Naive Nivo<br>Mono non-BM | N1 + I3 non-<br>BM   |  |  |
|-------------------------------------|---------------------------|----------------------|--|--|
| Subject group type                  | Subject analysis set      | Subject analysis set |  |  |
| Number of subjects analysed         | 35                        | 40                   |  |  |
| Units: Percentage of positive cells |                           |                      |  |  |
| median (standard deviation)         |                           |                      |  |  |
| Percent CD8 Baseline                | 5.210 (± 11.288)          | 4.230 (± 9.844)      |  |  |
| Percent positive CD8 Week 2         | 10.100 (± 10.909)         | 9.125 (± 18.654)     |  |  |
| Percent positive CD8 Week 4         | 18.435 (± 17.108)         | 34.785 (± 13.856)    |  |  |
| Percent CD4 Baseline                | 0.870 (± 3.727)           | 1.510 (± 6.023)      |  |  |
| Percent positive CD4 Week 2         | 4.210 (± 5.029)           | 5.990 (± 9.602)      |  |  |
| Percent positive CD4 Week 4         | 1.585 (± 3.071)           | 10.155 (± 12.707)    |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Safety and tolerability of Nivolumab, Ipilimumab and Nivolumab in combination with Ipilimumab as measured by the number of deaths and AEs

|                 |  |
|-----------------|--|
| End point title | Safety and tolerability of Nivolumab, Ipilimumab and Nivolumab in combination with Ipilimumab as measured by the number of deaths and AEs <sup>[5]</sup> |
|-----------------|--|

End point description:

The assessment of safety was based on frequency of deaths and adverse events (AEs). AEs were graded for severity according to the NCI CTCAE version 4.0.

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

End point timeframe:

Includes events reported between first dose and up to 100 days after last dose of study medication (up to approximately 2 years).

Notes:

[5] - 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: All participants listed in the baseline period who received treatment per the protocol are reported in the subject analysis sets which are subsets of the full population.

| End point values                                      | N1 30M + I3<br>30M non-BM | N3 30M non-<br>BM | N3 30M BM       | N1 60M + I3<br>90M   |
|---|---------------------------|-------------------|-----------------|----------------------|
| Subject group type                                    | Reporting group           | Reporting group   | Reporting group | Subject analysis set |
| Number of subjects analysed                           | 25                        | 11                | 10              | 27                   |
| Units: Events   |                           |                   |                 |                      |
| Participants who died                                 | 14                        | 4                 | 4               | 11                   |
| Participants who died within 30 days of<br>last dose  | 0                         | 0                 | 0               | 4                    |
| Participants who died within 100 days of<br>last dose | 0                         | 1                 | 2               | 5                    |
| Participants with an AE                               | 25                        | 11                | 10              | 27                   |

| End point values                                      | N3 60M Naive         | N3 60M PROG          | N1 30M + I3<br>30M BM |  |
|---|----------------------|----------------------|-----------------------|--|
| Subject group type                                    | Subject analysis set | Subject analysis set | Subject analysis set  |  |
| Number of subjects analysed                           | 41                   | 44                   | 10                    |  |
| Units: Events   |                      |                      |                       |  |
| Participants who died                                 | 26                   | 25                   | 2                     |  |
| Participants who died within 30 days of<br>last dose  | 3                    | 2                    | 1                     |  |
| Participants who died within 100 days of<br>last dose | 5                    | 8                    | 2                     |  |
| Participants with an AE                               | 41                   | 44                   | 10                    |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Laboratory Abnormalities in Specific Liver Tests

End point title Number of Laboratory Abnormalities in Specific Liver Tests<sup>[6]</sup>

End point description:

Abnormalities in hepatic parameters measured included those in aspartate aminotransferase (AST), alanine aminotransferase (ALT) and total bilirubin, with respect to upper limit of normal (ULN)

End point type Secondary

End point timeframe:

101-120 days after last dose.

Notes:

[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: All participants listed in the baseline period who received treatment per the protocol are reported in the subject analysis sets which are subsets of the full population.

| End point values            | N1 30M + I3<br>30M non-BM | N3 30M non-<br>BM | N3 30M BM       | N3 60M PROG          |
|-----------------------------|---------------------------|-------------------|-----------------|----------------------|
| Subject group type          | Reporting group           | Reporting group   | Reporting group | Subject analysis set |
| Number of subjects analysed | 25                        | 11                | 10              | 44                   |
| Units: Events               |                           |                   |                 |                      |
| ALT OR AST > 3XULN          | 5                         | 0                 | 0               | 4                    |
| ALT OR AST > 5XULN          | 4                         | 0                 | 0               | 2                    |
| ALT OR AST > 10XULN         | 2                         | 0                 | 0               | 0                    |

|  |   |   |   |   |
|--|---|---|---|---|
| ALT OR AST > 20XULN                                | 0 | 0 | 0 | 0 |
| TOTAL BILIRUBIN > 2XULN                            | 1 | 0 | 0 | 0 |
| ALT/AST ELEV>3XULN;TOTAL BILIRUBIN>2XULN IN 1 DAY  | 1 | 0 | 0 | 0 |
| ALT/AST ELEV>3XULN;TOTAL BILIRUBIN>2XULN IN 30 DAY | 1 | 0 | 0 | 0 |

| End point values                                   | N1 30M + I3<br>30M BM | N3 60M NAIVE         | N1 60M +I3<br>90M    |  |
|--|-----------------------|----------------------|----------------------|--|
| Subject group type                                 | Subject analysis set  | Subject analysis set | Subject analysis set |  |
| Number of subjects analysed                        | 10                    | 41                   | 27                   |  |
| Units: Events                                      |                       |                      |                      |  |
| ALT OR AST > 3XULN                                 | 3                     | 2                    | 8                    |  |
| ALT OR AST> 5XULN                                  | 1                     | 1                    | 6                    |  |
| ALT OR AST> 10XULN                                 | 1                     | 1                    | 3                    |  |
| ALT OR AST > 20XULN                                | 1                     | 0                    | 1                    |  |
| TOTAL BILIRUBIN > 2XULN                            | 2                     | 0                    | 2                    |  |
| ALT/AST ELEV>3XULN;TOTAL BILIRUBIN>2XULN IN 1 DAY  | 1                     | 0                    | 2                    |  |
| ALT/AST ELEV>3XULN;TOTAL BILIRUBIN>2XULN IN 30 DAY | 1                     | 0                    | 2                    |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Laboratory Abnormalities in Specific Thyroid Tests

|                 |   |
|-----------------|---|
| End point title | Number of Laboratory Abnormalities in Specific Thyroid Tests <sup>[7]</sup> |
|-----------------|---|

End point description:

Abnormalities in thyroid parameters measured included those in thyroid stimulating hormone (TSH) levels with respect to upper limit of normal (ULN) and lower limit of normal (LLN)

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

End point timeframe:

101-120 days after last dose.

Notes:

[7] - 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: All participants listed in the baseline period who received treatment per the protocol are reported in the subject analysis sets which are subsets of the full population.

| End point values                                  | N1 30M + I3<br>30M non-BM | N3 30M non-<br>BM | N3 30M BM       | N1 30M + I3<br>30M BM |
|---|---------------------------|-------------------|-----------------|-----------------------|
| Subject group type                                | Reporting group           | Reporting group   | Reporting group | Subject analysis set  |
| Number of subjects analysed                       | 25                        | 11                | 8               | 10                    |
| Units: Events                                     |                           |                   |                 |                       |
| TSH > ULN   | 7                         | 1                 | 4               | 3                     |
| TSH > ULN WITH TSH <= ULN AT BASELINE             | 4                         | 1                 | 2               | 3                     |
| TSH >ULN WITH ATLEAST ONE FT3/FT4 TEST VALUE <LLN | 3                         | 0                 | 2               | 2                     |

|  |    |   |   |   |
|--|----|---|---|---|
| TSH >ULN WITH ALL OTHER FT3/FT4 TEST VALUES >= LLN | 0  | 0 | 0 | 0 |
| TSH > ULN WITH FT3/FT4 TEST MISSING                | 4  | 1 | 2 | 1 |
| TSH < LLN  | 12 | 2 | 5 | 6 |
| TSH <LLN WITH TSH >= LLN AT BASELINE               | 12 | 2 | 5 | 6 |
| TSH <LLN WITH ATLEAST ONE FT3/FT4 TEST VALUE > ULN | 4  | 0 | 2 | 2 |
| TSH <LLN WITH ALL OTHER FT3/FT4 TEST VALUES <= ULN | 1  | 0 | 1 | 0 |
| TSH < LLN WITH FT3/FT4 TEST MISSING                | 7  | 2 | 2 | 4 |

| End point values                                   | N3 60M NAIVE         | N3 60M PROG          | N1 60M +I3 90M       |  |
|--|----------------------|----------------------|----------------------|--|
| Subject group type                                 | Subject analysis set | Subject analysis set | Subject analysis set |  |
| Number of subjects analysed                        | 29                   | 33                   | 21                   |  |
| Units: Events                                      |                      |                      |                      |  |
| TSH > ULN  | 9                    | 16                   | 7                    |  |
| TSH > ULN WITH TSH <= ULN AT BASELINE              | 4                    | 9                    | 7                    |  |
| TSH >ULN WITH ATLEAST ONE FT3/FT4 TEST VALUE <LLN  | 0                    | 0                    | 3                    |  |
| TSH >ULN WITH ALL OTHER FT3/FT4 TEST VALUES >= LLN | 0                    | 0                    | 0                    |  |
| TSH > ULN WITH FT3/FT4 TEST MISSING                | 9                    | 16                   | 4                    |  |
| TSH < LLN  | 3                    | 4                    | 11                   |  |
| TSH <LLN WITH TSH >= LLN AT BASELINE               | 3                    | 4                    | 11                   |  |
| TSH <LLN WITH ATLEAST ONE FT3/FT4 TEST VALUE > ULN | 0                    | 0                    | 5                    |  |
| TSH <LLN WITH ALL OTHER FT3/FT4 TEST VALUES <= ULN | 0                    | 0                    | 3                    |  |
| TSH < LLN WITH FT3/FT4 TEST MISSING                | 3                    | 4                    | 3                    |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Antitumor Activity of Nivolumab and Nivolumab in combination with Ipilimumab as measured by the objective response rate (ORR)

|                 |  |
|-----------------|--|
| End point title | Antitumor Activity of Nivolumab and Nivolumab in combination with Ipilimumab as measured by the objective response rate (ORR) <sup>[8]</sup> |
|-----------------|--|

End point description:

The objective response rate (ORR) was defined as the number of subjects with a best overall response (BOR) of a complete response (CR) or partial response (PR) divided by the number of randomized subjects in the population of interest (eg, all treated subjects or response-evaluable subjects). The BOR was defined as the subject's best response designation, over the study as a whole, recorded between the date of first study drug administration and the date of objectively documented progression per RECIST 1.1, with subsequent confirmation, or date of subsequent anti-cancer therapy, whichever

occurred first in the study.

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

End point timeframe:

Approximately every 8 weeks until disease progression and in follow-up if no progression (up to approximately 2 years)

Notes:

[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: All participants listed in the baseline period who received treatment per the protocol are reported in the subject analysis sets which are subsets of the full population.

| End point values                  | N3 60M Prog         | N1 30M + I3 30M non-BM | N3 30M non-BM      | N3 30M BM           |
|-----------------------------------|---------------------|------------------------|--------------------|---------------------|
| Subject group type                | Reporting group     | Reporting group        | Reporting group    | Reporting group     |
| Number of subjects analysed       | 44                  | 25                     | 11                 | 10                  |
| Units: Percentage of participants |                     |                        |                    |                     |
| number (confidence interval 95%)  | 22.7 (11.5 to 37.8) | 40.0 (21.1 to 61.3)    | 27.3 (6.0 to 61.0) | 60.0 (26.2 to 87.8) |

| End point values                  | N3 60M Naive         | N1 30M + I3 30M BM   | N1 60M+I3 90M        |  |
|-----------------------------------|----------------------|----------------------|----------------------|--|
| Subject group type                | Subject analysis set | Subject analysis set | Subject analysis set |  |
| Number of subjects analysed       | 41                   | 10                   | 27                   |  |
| Units: Percentage of participants |                      |                      |                      |  |
| number (confidence interval 95%)  | 31.7 (18.1 to 48.1)  | 70.0 (34.8 to 93.3)  | 44.4 (25.5 to 64.7)  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Antitumor Activity of Nivolumab and Nivolumab in combination with Ipilimumab as measured by the median duration of response (mDOR)

|                 |   |
|-----------------|---|
| End point title | Antitumor Activity of Nivolumab and Nivolumab in combination with Ipilimumab as measured by the median duration of response (mDOR) <sup>[9]</sup> |
|-----------------|---|

End point description:

Median duration of response (mDOR) was calculated for subjects with BOR of CR or PR only, and is defined as time between the date of first documented objective response and the date of the first subsequent disease progression or death, whichever occurred first, if death occurred within 100 days after last dose of study medication.

"999"=N/A

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

End point timeframe:

2 years from the first dose of treatment

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: All participants listed in the baseline period who received treatment per the protocol are reported in the subject analysis sets which are subsets of the full population.

| End point values                 | N3 30M BM            | N1 60M + I3 90M      | N3 60M Naive         | N3 60M PROG          |
|----------------------------------|----------------------|----------------------|----------------------|----------------------|
| Subject group type               | Reporting group      | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed      | 10                   | 27                   | 41                   | 44                   |
| Units: Months                    |                      |                      |                      |                      |
| median (confidence interval 95%) | 20.27 (13.57 to 999) | 999 (5.85 to 999)    | 16.59 (7.29 to 999)  | 999 (5.55 to 999)    |

| End point values                 | N1 30M + I3 30M BM   | N1 30M + I3 30M NON-BM | N3 30M NON-BM        |  |
|----------------------------------|----------------------|------------------------|----------------------|--|
| Subject group type               | Subject analysis set | Subject analysis set   | Subject analysis set |  |
| Number of subjects analysed      | 10                   | 25                     | 11                   |  |
| Units: Months                    |                      |                        |                      |  |
| median (confidence interval 95%) | 999 (22.01 to 999)   | 26.25 (7.85 to 999)    | 999 (3.71 to 999)    |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Antitumor Activity of Nivolumab and Nivolumab in combination with Ipilimumab as measured by the median time to response (mTTR)

|                 |  |
|-----------------|--|
| End point title | Antitumor Activity of Nivolumab and Nivolumab in combination with Ipilimumab as measured by the median time to response (mTTR) <sup>[10]</sup> |
|-----------------|--|

End point description:

Median time to response (mTTR) for a participant with a BOR of CR or PR is defined as the time from the first dosing date to the date of the first documented objective response (CR or PR).

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

End point timeframe:

2 years from the first dose of treatment

Notes:

[10] - 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: All participants listed in the baseline period who received treatment per the protocol are reported in the subject analysis sets which are subsets of the full population.

| End point values                 | N3 30M BM           | N1 60M + I3 90M      | N3 60M Naive         | N3 60M PROG          |
|----------------------------------|---------------------|----------------------|----------------------|----------------------|
| Subject group type               | Reporting group     | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed      | 10                  | 27                   | 41                   | 44                   |
| Units: Months                    |                     |                      |                      |                      |
| median (confidence interval 95%) | 2.14 (1.25 to 4.99) | 1.41 (1.28 to 1.87)  | 1.87 (1.77 to 3.71)  | 2.78 (1.84 to 14.59) |

| End point values | N1 30M + I3 30M BM | N1 30M + I3 30M NON-BM | N3 30M NON-BM |  |
|------------------|--------------------|------------------------|---------------|--|
|------------------|--------------------|------------------------|---------------|--|



|                                  |                      |                      |                      |  |
|----------------------------------|----------------------|----------------------|----------------------|--|
| Subject group type               | Subject analysis set | Subject analysis set | Subject analysis set |  |
| Number of subjects analysed      | 10                   | 25                   | 11                   |  |
| Units: Months                    |                      |                      |                      |  |
| median (confidence interval 95%) | 1.71 (1.38 to 7.43)  | 2.51 (1.28 to 2.86)  | 1.41 (1.41 to 6.90)  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Antitumor Activity of Nivolumab and Nivolumab in combination with Ipilimumab as measured by the progression free survival rate (PFSR)

|                 |   |
|-----------------|---|
| End point title | Antitumor Activity of Nivolumab and Nivolumab in combination with Ipilimumab as measured by the progression free survival rate (PFSR) <sup>[11]</sup> |
|-----------------|---|

End point description:

The progression free survival rate (PFSR) for a subject was defined as the time from the date of first dose of study medication to the date of the first documented disease progression, or death due to any cause, whichever occurred first, if death occurred within 100 days after last dose of study medication.

"999"=N/A

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

End point timeframe:

2 years from the first dose of treatment

Notes:

[11] - 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: All participants listed in the baseline period who received treatment per the protocol are reported in the subject analysis sets which are subsets of the full population.

| End point values                 | N3 30M BM           | N1 60M + I3 90M      | N3 60M Naive         | N3 60M PROG          |
|----------------------------------|---------------------|----------------------|----------------------|----------------------|
| Subject group type               | Reporting group     | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed      | 10                  | 27                   | 41                   | 44                   |
| Units: Percentage                |                     |                      |                      |                      |
| median (confidence interval 95%) | 23.00 (0.85 to 999) | 7.00 (1.41 to 999)   | 3.68 (1.84 to 7.36)  | 5.62 (1.87 to 9.66)  |

| End point values                 | N1 30M + I3 30M BM   | N1 30M + I3 30M NON-BM | N3 30M NON-BM        |  |
|----------------------------------|----------------------|------------------------|----------------------|--|
| Subject group type               | Subject analysis set | Subject analysis set   | Subject analysis set |  |
| Number of subjects analysed      | 10                   | 25                     | 11                   |  |
| Units: Percentage                |                      |                        |                      |  |
| median (confidence interval 95%) | 999 (1.18 to 999)    | 9.69 (1.94 to 29.01)   | 4.93 (1.41 to 999)   |  |

## Statistical analyses

**Secondary: Immunogenicity of Nivolumab and Nivolumab in combination with Ipilimumab as measured by the number of serum anti-drug antibody (ADA) positive participants and the number of neutralizing ADA positive participants**

|                 |   |
|-----------------|---|
| End point title | Immunogenicity of Nivolumab and Nivolumab in combination with Ipilimumab as measured by the number of serum anti-drug antibody (ADA) positive participants and the number of neutralizing ADA positive participants <sup>[12]</sup> |
|-----------------|---|

End point description:

Time Frame: Part 1: Day 1, Day 15, Day 43 of cycle 1, Day 1 of cycle 2, Day 15 of cycle 3, every 16 weeks after cycle 3 up to 2 years, follow-up visit 1 (40-60 days after last treatment), and follow-up visit 2 (101-120 days since last treatment) Part 2, 3 and 4: Weeks 1, 3, 4, 7, 9, 10, 13, 25, 53, 79, 95 follow-up visit 1 (40-60 days after last treatment), and follow-up visit 2 (101-120 days since last treatment).

"999"=N/A

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

End point timeframe:

Up to follow-up visit 2 (101-120 days since last treatment)

Notes:

[12] - 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: All participants listed in the baseline period who received treatment per the protocol are reported in the subject analysis sets which are subsets of the full population.

| End point values            | N3 30M non-BM   | N3 30M BM       | N3 60M NAIVE         | N3 60M PROG          |
|-----------------------------|-----------------|-----------------|----------------------|----------------------|
| Subject group type          | Reporting group | Reporting group | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 11              | 7               | 38                   | 42                   |
| Units: Participants         |                 |                 |                      |                      |
| ADA positive                | 1               | 1               | 2                    | 5                    |
| Neutralizing ADA positive   | 0               | 0               | 0                    | 0                    |

| End point values            | N1 60M + I3<br>(Nivo ADA) | N1 60M + I3<br>90M (Ipi ADA) | N1 30M + I3<br>30M Non-BM<br>(Nivo ADA) | N1 30M + I3<br>30M Non-BM<br>(Ipi ADA) |
|-----------------------------|---------------------------|------------------------------|---|--|
| Subject group type          | Subject analysis set      | Subject analysis set         | Subject analysis set                    | Subject analysis set                   |
| Number of subjects analysed | 22                        | 22                           | 24                                      | 23                                     |
| Units: Participants         |                           |                              |   |  |
| ADA positive                | 10                        | 1                            | 16                                      | 4                                      |
| Neutralizing ADA positive   | 0                         | 0                            | 1                                       | 0                                      |

| End point values            | N1 30M + I3<br>30M (Nivo<br>ADA) | N1 30M + I3<br>30M (Ipi ADA) | Total (Nivo<br>ADA)  | Total (Ipi ADA)      |
|-----------------------------|----------------------------------|------------------------------|----------------------|----------------------|
| Subject group type          | Subject analysis set             | Subject analysis set         | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 10                               | 9                            | 154                  | 54                   |
| Units: Participants         |                                  |                              |                      |                      |
| ADA positive                | 7                                | 0                            | 42                   | 5                    |

|                           |   |     |   |   |
|---------------------------|---|-----|---|---|
| Neutralizing ADA positive | 2 | 999 | 3 | 0 |
|---------------------------|---|-----|---|---|

## Statistical analyses

No statistical analyses for this end point

### Secondary: Association between Programmed cell death ligand 1 (PD-L1) and clinical efficacy measures such as Objective Response Rate (PD-L1 ORR)

|                 |   |
|-----------------|---|
| End point title | Association between Programmed cell death ligand 1 (PD-L1) and clinical efficacy measures such as Objective Response Rate (PD-L1 ORR) <sup>[13]</sup> |
|-----------------|---|

End point description:

For immunohistochemistry (IHC) measurements, to explore the PD-L1 expression as a potential predictive marker of clinical activity, PD-L1 expression status were derived from percent of tumor cells exhibiting cell surface staining for PD-L1 at baseline and/or in archived biopsy samples using verified and/or validated assays. In the case of multiple specimens, a subject would be identified as PD-L1 expression levels  $\geq x\%$ , where  $x\%$  can be 10%, 5%, and/or 1% in any of the baseline and/or archived specimens. The association between PD-L1 expression status and/or level and clinical efficacy measures was assessed. The objective response rate (ORR) was defined as the number of subjects with a best overall response (BOR) of a complete response (CR) or partial response (PR) divided by the number of randomized subjects in the population of interest (all response-evaluable participants).

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

End point timeframe:

2 years from first dose of treatment; Assessed up to September 2017

Notes:

[13] - 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: All participants listed in the baseline period who received treatment per the protocol are reported in the subject analysis sets which are subsets of the full population.

| End point values                              | N1 60M + I3 90M, W2   | N1 60M + I3 90M, W4 | N3 60M NAIVE, W4     | N3 60M PROG, W4      |
|---|-----------------------|---------------------|----------------------|----------------------|
| Subject group type                            | Reporting group       | Reporting group     | Subject analysis set | Subject analysis set |
| Number of subjects analysed                   | 11                    | 10                  | 39                   | 36                   |
| Units: Percentage                             |                       |                     |                      |                      |
| number (confidence interval 95%)              |                       |                     |                      |                      |
| STTU 1 - 1% Level PD-L1 Status: Met criteria  | 85.7 (42.1 to 99.6)   | 50.0 (11.8 to 88.2) | 40.0 (19.1 to 63.9)  | 35.3 (14.2 to 61.7)  |
| STTU 1 - 5% Level PD-L1 Status: Met criteria  | 80.0 (28.4 to 99.5)   | 60.0 (14.7 to 94.7) | 40.0 (12.2 to 73.8)  | 33.3 (7.5 to 70.1)   |
| STTU 1 - 10% Level PD-L1 Status: Met criteria | 100.0 (29.2 to 100.0) | 75.0 (19.4 to 99.4) | 42.9 (9.9 to 81.6)   | 20.0 (0.5 to 71.6)   |

| End point values                 | N1 60M + I3 90M, WU  | N1 30M + I3 30M NON-BM | N3 30M NON-BM, W2    | N1 30M + I3 30M BM, W2 |
|----------------------------------|----------------------|------------------------|----------------------|------------------------|
| Subject group type               | Subject analysis set | Subject analysis set   | Subject analysis set | Subject analysis set   |
| Number of subjects analysed      | 6                    | 22                     | 9                    | 4                      |
| Units: Percentage                |                      |                        |                      |                        |
| number (confidence interval 95%) |                      |                        |                      |                        |

|   |                      |                     |                      |                       |
|---|----------------------|---------------------|----------------------|-----------------------|
| STTU 1 - 1% Level PD-L1 Status: Met criteria  | 50.0 (1.3 to 98.7)   | 63.6 (30.8 to 89.1) | 40.0 (5.3 to 85.3)   | 100.0 (15.8 to 100.0) |
| STTU 1 - 5% Level PD-L1 Status: Met criteria  | 100.0 (2.5 to 100.0) | 71.4 (29.0 to 96.3) | 50.0 (1.3 to 98.7)   | 100.0 (15.8 to 100.0) |
| STTU 1 - 10% Level PD-L1 Status: Met criteria | 100.0 (2.5 to 100.0) | 66.7 (9.4 to 99.2)  | 100.0 (2.5 to 100.0) | 100.0 (15.8 to 100.0) |

| End point values                              | N3 30M BM, W2        | N3 60M, W4           | N3 30M, W2            | N1 + I3, W2          |
|---|----------------------|----------------------|-----------------------|----------------------|
| Subject group type                            | Subject analysis set | Subject analysis set | Subject analysis set  | Subject analysis set |
| Number of subjects analysed                   | 3                    | 75                   | 12                    | 37                   |
| Units: Percentage                             |                      |                      |                       |                      |
| number (confidence interval 95%)              |                      |                      |                       |                      |
| STTU 1 - 1% Level PD-L1 Status: Met criteria  | 100.0 (2.5 to 100.0) | 37.8 (22.5 to 55.2)  | 50.0 (11.8 to 88.2)   | 75.0 (50.9 to 91.3)  |
| STTU 1 - 5% Level PD-L1 Status: Met criteria  | 100.0 (2.5 to 100.0) | 36.8 (16.3 to 61.6)  | 66.7 (9.4 to 99.2)    | 78.6 (49.2 to 95.3)  |
| STTU 1 - 10% Level PD-L1 Status: Met criteria | 100.0 (2.5 to 100.0) | 33.3 (9.9 to 65.1)   | 100.0 (15.8 to 100.0) | 87.5 (47.3 to 99.7)  |

| End point values                              | N1 + I3 W2, NON-BM   | N3 NAIVE, NON-BM     | N1 + I3 NON-BM       | Total                |
|---|----------------------|----------------------|----------------------|----------------------|
| Subject group type                            | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed                   | 33                   | 48                   | 49                   | 140                  |
| Units: Percentage                             |                      |                      |                      |                      |
| number (confidence interval 95%)              |                      |                      |                      |                      |
| STTU 1 - 1% Level PD-L1 Status: Met criteria  | 72.2 (46.5 to 90.3)  | 40.0 (21.1 to 61.3)  | 65.4 (44.3 to 82.8)  | 50.7 (38.6 to 62.8)  |
| STTU 1 - 5% Level PD-L1 Status: Met criteria  | 75.0 (42.8 to 94.5)  | 41.7 (15.2 to 72.3)  | 72.2 (46.5 to 90.3)  | 57.1 (41.0 to 72.3)  |
| STTU 1 - 10% Level PD-L1 Status: Met criteria | 83.3 (35.9 to 99.6)  | 50.0 (15.7 to 84.3)  | 81.8 (48.2 to 97.7)  | 63.0 (42.4 to 80.6)  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Association between Programmed cell death ligand 1 (PD-L1) and clinical efficacy measures such as the Duration of Response (PD-L1 DOR)

|                 |  |
|-----------------|--|
| End point title | Association between Programmed cell death ligand 1 (PD-L1) and clinical efficacy measures such as the Duration of Response (PD-L1 DOR) <sup>[14]</sup> |
|-----------------|--|

End point description:

For immunohistochemistry (IHC) measurements, to explore the PD-L1 expression as a potential predictive marker of clinical activity, PD-L1 expression status were derived from percent of tumor cells exhibiting cell surface staining for PD-L1 at baseline and/or in archived biopsy samples using verified and/or validated assays. In the case of multiple specimens, a subject would be identified as PD-L1 expression levels  $\geq x\%$ , where  $x\%$  can be 10%, 5%, and/or 1% in any of the baseline and/or archived specimens. Median duration of response (mDOR) was calculated for all response-evaluable participants with best overall response of CR or PR only, and is defined as time between the date of first documented

objective response and the date of the first subsequent disease progression or death, whichever occurred first, if death occurred within 100 days after last dose of study medication.

"999"=N/A

|   |           |
|---|-----------|
| End point type  | Secondary |
| End point timeframe:  |           |
| 2 years from first dose of treatment; Assessed up to September 2017 |           |

Notes:

[14] - 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: All participants listed in the baseline period who received treatment per the protocol are reported in the subject analysis sets which are subsets of the full population.

| End point values                              | N1 60M + I3 90M, W2 | N1 60M + I3 90M, W4 | N3 60M NAIVE, W4       | N3 60M PROG, W4      |
|---|---------------------|---------------------|------------------------|----------------------|
| Subject group type                            | Reporting group     | Reporting group     | Subject analysis set   | Subject analysis set |
| Number of subjects analysed                   | 11                  | 10                  | 39                     | 36                   |
| Units: Months                                 |                     |                     |                        |                      |
| median (confidence interval 95%)              |                     |                     |                        |                      |
| STTU 1 - 1% Level PD-L1 Status: Met criteria  | 999 (2.96 to 999)   | 999 (999 to 999)    | 15.21 (4.60 to 18.20)  | 999 (15.57 to 999)   |
| STTU 1 - 5% Level PD-L1 Status: Met criteria  | 999 (2.96 to 999)   | 999 (999 to 999)    | 15.21 (11.50 to 16.59) | 999 (15.57 to 999)   |
| STTU 1 - 10% Level PD-L1 Status: Met criteria | 999 (2.96 to 999)   | 999 (999 to 999)    | 15.90 (15.21 to 16.59) | 15.57 (-999 to 999)  |

| End point values                              | N1 60M + I3 90M, WU  | N1 30M + I3 30M NON-BM | N3 30M NON-BM, W2    | N1 30M + I3 30M BM, W2 |
|---|----------------------|------------------------|----------------------|------------------------|
| Subject group type                            | Subject analysis set | Subject analysis set   | Subject analysis set | Subject analysis set   |
| Number of subjects analysed                   | 6                    | 22                     | 9                    | 4                      |
| Units: Months                                 |                      |                        |                      |                        |
| median (confidence interval 95%)              |                      |                        |                      |                        |
| STTU 1 - 1% Level PD-L1 Status: Met criteria  | 999 (999 to 999)     | 26.25 (8.31 to 999)    | 999 (3.71 to 999)    | 22.01 (-999 to 999)    |
| STTU 1 - 5% Level PD-L1 Status: Met criteria  | 999 (999 to 999)     | 26.25 (8.31 to 999)    | 999 (3.71 to 999)    | 22.01 (-999 to 999)    |
| STTU 1 - 10% Level PD-L1 Status: Met criteria | 999 (999 to 999)     | 999 (999 to 999)       | 999 (999 to 999)     | 22.01 (-999 to 999)    |

| End point values                              | N3 30M BM, W2        | N3 60M, W4             | N3 30M, W2           | N1 + I3, W2          |
|---|----------------------|------------------------|----------------------|----------------------|
| Subject group type                            | Subject analysis set | Subject analysis set   | Subject analysis set | Subject analysis set |
| Number of subjects analysed                   | 3                    | 75                     | 12                   | 37                   |
| Units: Months                                 |                      |                        |                      |                      |
| median (confidence interval 95%)              |                      |                        |                      |                      |
| STTU 1 - 1% Level PD-L1 Status: Met criteria  | 999 (999 to 999)     | 16.59 (11.50 to 999)   | 999 (3.71 to 999)    | 26.25 (22.01 to 999) |
| STTU 1 - 5% Level PD-L1 Status: Met criteria  | 999 (999 to 999)     | 16.59 (11.50 to 999)   | 999 (999 to 999)     | 26.25 (8.31 to 999)  |
| STTU 1 - 10% Level PD-L1 Status: Met criteria | 999 (999 to 999)     | 15.57 (15.21 to 16.59) | 999 (999 to 999)     | 999 (2.96 to 999)    |

| End point values                              | N1 + I3 W2, NON-BM   | N3 NAIVE, NON-BM     | N1 + I3 NON-BM       | Total                |
|---|----------------------|----------------------|----------------------|----------------------|
| Subject group type                            | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed                   | 33                   | 48                   | 49                   | 140                  |
| Units: Months                                 |                      |                      |                      |                      |
| median (confidence interval 95%)              |                      |                      |                      |                      |
| STTU 1 - 1% Level PD-L1 Status: Met criteria  | 999 (8.31 to 999)    | 15.21 (3.71 to 999)  | 999 (26.25 to 999)   | 26.25 (16.59 to 999) |
| STTU 1 - 5% Level PD-L1 Status: Met criteria  | 999 (2.96 to 999)    | 16.59 (11.50 to 999) | 999 (8.31 to 999)    | 26.25 (15.57 to 999) |
| STTU 1 - 10% Level PD-L1 Status: Met criteria | 999 (2.96 to 999)    | 16.59 (15.21 to 999) | 999 (2.96 to 999)    | 999 (15.57 to 999)   |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Association between Programmed cell death ligand 1 (PD-L1) and clinical efficacy measures such as Progression Free Survival (PD-L1 PFS)

|                 |   |
|-----------------|---|
| End point title | Association between Programmed cell death ligand 1 (PD-L1) and clinical efficacy measures such as Progression Free Survival (PD-L1 PFS) <sup>[15]</sup> |
|-----------------|---|

End point description:

For immunohistochemistry (IHC) measurements, to explore the PD-L1 expression as a potential predictive marker of clinical activity, PD-L1 expression status were derived from percent of tumor cells exhibiting cell surface staining for PD-L1 at baseline and/or in archived biopsy samples using verified and/or validated assays. In the case of multiple specimens, a subject would be identified as PD-L1 expression levels  $\geq x\%$ , where  $x\%$  can be 10%, 5%, and/or 1% in any of the baseline and/or archived specimens. The association between PD-L1 expression status and/or level and clinical efficacy measures was assessed. The progression free survival rate (PFSR) for a subject was defined as the time from the date of first dose of study medication to the date of the first documented disease progression, or death due to any cause, whichever occurred first, if death occurred within 100 days after last dose of study medication.

"999"=N/A

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

End point timeframe:

2 years from first dose of treatment; Assessed up to September 2017

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: All participants listed in the baseline period who received treatment per the protocol are reported in the subject analysis sets which are subsets of the full population.

| End point values                 | N1 60M + I3 90M, W2 | N1 60M + I3 90M, W4 | N3 60M NAIVE, W4     | N3 60M PROG, W4      |
|----------------------------------|---------------------|---------------------|----------------------|----------------------|
| Subject group type               | Reporting group     | Reporting group     | Subject analysis set | Subject analysis set |
| Number of subjects analysed      | 11                  | 10                  | 39                   | 36                   |
| Units: Months                    |                     |                     |                      |                      |
| median (confidence interval 95%) |                     |                     |                      |                      |

|   |                   |                   |                      |                       |
|---|-------------------|-------------------|----------------------|-----------------------|
| STTU 1 - 1% Level PD-L1 Status: Met criteria  | 999 (1.22 to 999) | 999 (0.85 to 999) | 4.50 (1.84 to 15.18) | 9.66 (3.71 to 999)    |
| STTU 1 - 5% Level PD-L1 Status: Met criteria  | 999 (1.22 to 999) | 999 (0.85 to 999) | 6.28 (0.33 to 17.05) | 19.29 (1.77 to 999)   |
| STTU 1 - 10% Level PD-L1 Status: Met criteria | 999 (4.17 to 999) | 999 (1.64 to 999) | 5.36 (0.33 to 18.40) | 19.29 (1.77 to 19.29) |

| End point values                              | N1 60M + I3 90M, WU  | N1 30M + I3 30M NON-BM | N3 30M NON-BM, W2    | N1 30M + I3 30M BM, W2 |
|---|----------------------|------------------------|----------------------|------------------------|
| Subject group type                            | Subject analysis set | Subject analysis set   | Subject analysis set | Subject analysis set   |
| Number of subjects analysed                   | 6                    | 22                     | 9                    | 4                      |
| Units: Months                                 |                      |                        |                      |                        |
| median (confidence interval 95%)              |                      |                        |                      |                        |
| STTU 1 - 1% Level PD-L1 Status: Met criteria  | 999 (0.76 to 999)    | 29.01 (1.94 to 29.01)  | 8.77 (1.22 to 999)   | 999 (23.95 to 999)     |
| STTU 1 - 5% Level PD-L1 Status: Met criteria  | 999 (999 to 999)     | 29.01 (1.94 to 29.01)  | 999 (1.22 to 999)    | 999 (23.95 to 999)     |
| STTU 1 - 10% Level PD-L1 Status: Met criteria | 999 (999 to 999)     | 999 (1.94 to 999)      | 999 (999 to 999)     | 999 (23.95 to 999)     |

| End point values                              | N3 30M BM, W2        | N3 60M, W4           | N3 30M, W2           | N1 + I3, W2          |
|---|----------------------|----------------------|----------------------|----------------------|
| Subject group type                            | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed                   | 3                    | 75                   | 12                   | 37                   |
| Units: Months                                 |                      |                      |                      |                      |
| median (confidence interval 95%)              |                      |                      |                      |                      |
| STTU 1 - 1% Level PD-L1 Status: Met criteria  | 999 (999 to 999)     | 6.24 (3.65 to 17.05) | 8.77 (1.22 to 999)   | 29.01 (4.17 to 999)  |
| STTU 1 - 5% Level PD-L1 Status: Met criteria  | 999 (999 to 999)     | 7.20 (1.87 to 18.40) | 999 (1.22 to 999)    | 29.01 (3.02 to 999)  |
| STTU 1 - 10% Level PD-L1 Status: Met criteria | 999 (999 to 999)     | 6.24 (1.71 to 18.40) | 999 (999 to 999)     | 999 (1.94 to 999)    |

| End point values                              | N1 + I3 W2, NON-BM   | N3 NAIVE, NON-BM     | N1 + I3 NON-BM       | Total                 |
|---|----------------------|----------------------|----------------------|-----------------------|
| Subject group type                            | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set  |
| Number of subjects analysed                   | 33                   | 48                   | 49                   | 140                   |
| Units: Months                                 |                      |                      |                      |                       |
| median (confidence interval 95%)              |                      |                      |                      |                       |
| STTU 1 - 1% Level PD-L1 Status: Met criteria  | 29.01 (3.02 to 999)  | 5.36 (1.94 to 10.94) | 29.01 (3.02 to 999)  | 10.58 (5.62 to 19.81) |
| STTU 1 - 5% Level PD-L1 Status: Met criteria  | 29.01 (1.94 to 999)  | 6.28 (1.22 to 17.05) | 29.01 (3.02 to 999)  | 17.05 (5.36 to 29.01) |
| STTU 1 - 10% Level PD-L1 Status: Met criteria | 999 (1.94 to 999)    | 11.20 (0.33 to 999)  | 999 (1.94 to 999)    | 19.29 (5.36 to 999)   |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Antitumor Activity of Nivolumab and Nivolumab in combination with Ipilimumab as measured by the Overall Survival Rate (OSR)

|                 |   |
|-----------------|---|
| End point title | Antitumor Activity of Nivolumab and Nivolumab in combination with Ipilimumab as measured by the Overall Survival Rate (OSR) <sup>[16]</sup> |
|-----------------|---|

End point description:

The proportion of subjects surviving to time t, where t is a specific length of time, eg, 12 months, which was determined by the available data for final analysis and was documented in the DPP. The proportion was calculated by the product-limit method (Kaplan-Meier estimate), which takes into account censored data. The overall survival rate (OSR) for a subject was defined as the time from the date of first dose of study medication to the date of death for any cause. A subject who had not died was censored at last known date alive

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

End point timeframe:

2 years from first dose of treatment; Assessed up to September 2017

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: All participants listed in the baseline period who received treatment per the protocol are reported in the subject analysis sets which are subsets of the full population.

| End point values                  | N3 30M BM           | N1 60M + I3 90M      | N3 60M Naive         | N3 60M PROG          |
|-----------------------------------|---------------------|----------------------|----------------------|----------------------|
| Subject group type                | Reporting group     | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed       | 10                  | 27                   | 41                   | 44                   |
| Units: Percentage of participants |                     |                      |                      |                      |
| median (confidence interval 95%)  |                     |                      |                      |                      |
| 3 months                          | 80.0 (40.9 to 94.6) | 85.2 (65.2 to 94.2)  | 92.7 (79.0 to 97.6)  | 90.8 (77.3 to 96.4)  |
| 6 months                          | 80.0 (40.9 to 94.6) | 81.5 (61.1 to 91.8)  | 85.3 (70.2 to 93.1)  | 78.9 (63.3 to 88.4)  |
| 9 months                          | 68.6 (30.5 to 88.7) | 81.5 (61.1 to 91.8)  | 75.0 (58.5 to 85.7)  | 71.7 (55.5 to 82.8)  |
| 12 months                         | 68.6 (30.5 to 88.7) | 77.6 (56.8 to 89.3)  | 72.4 (55.7 to 83.7)  | 64.5 (48.2 to 76.9)  |
| 24 months                         | 57.1 (21.7 to 81.5) | 69.6 (48.3 to 83.5)  | 51.0 (34.3 to 65.4)  | 46.8 (31.1 to 61.1)  |

| End point values                  | N1 30M + I3 30M BM   | N1 30M + I3 30M NON-BM | N3 30M NON-BM        | N1 + I3 NON-BM       |
|-----------------------------------|----------------------|------------------------|----------------------|----------------------|
| Subject group type                | Subject analysis set | Subject analysis set   | Subject analysis set | Subject analysis set |
| Number of subjects analysed       | 10                   | 25                     | 11                   | 52                   |
| Units: Percentage of participants |                      |                        |                      |                      |
| median (confidence interval 95%)  |                      |                        |                      |                      |
| 3 months                          | 90.0 (47.3 to 98.5)  | 100.0 (100.0 to 100.0) | 90.0 (47.3 to 98.5)  | 92.3 (80.8 to 97.0)  |
| 6 months                          | 90.0 (47.3 to 98.5)  | 100.0 (100.0 to 100.0) | 90.0 (47.3 to 98.5)  | 90.4 (78.4 to 95.9)  |
| 9 months                          | 90.0 (47.3 to 98.5)  | 88.0 (67.3 to 96.0)    | 90.0 (47.3 to 98.5)  | 84.6 (71.6 to 92.0)  |



|           |                     |                     |                     |                     |
|-----------|---------------------|---------------------|---------------------|---------------------|
| 12 months | 90.0 (47.3 to 98.5) | 88.0 (67.3 to 96.0) | 80.0 (40.9 to 94.6) | 82.6 (69.3 to 90.6) |
| 24 months | 80.0 (40.9 to 94.6) | 58.1 (36.0 to 75.0) | 58.3 (23.0 to 82.1) | 64.3 (49.3 to 75.8) |

| End point values                  | N3 NAIVE             | All N3               | N1 + I3              | Total                |
|-----------------------------------|----------------------|----------------------|----------------------|----------------------|
| Subject group type                | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed       | 62                   | 106                  | 62                   | 168                  |
| Units: Percentage of participants |                      |                      |                      |                      |
| median (confidence interval 95%)  |                      |                      |                      |                      |
| 3 months                          | 90.2 (79.6 to 95.5)  | 90.5 (83.0 to 94.8)  | 91.9 (81.7 to 96.6)  | 91.0 (85.5 to 94.5)  |
| 6 months                          | 85.3 (73.6 to 92.0)  | 82.6 (73.8 to 88.6)  | 90.3 (79.7 to 95.5)  | 85.5 (79.2 to 90.1)  |
| 9 months                          | 76.6 (63.7 to 85.4)  | 74.6 (64.9 to 81.9)  | 85.5 (74.0 to 92.2)  | 78.7 (71.6 to 84.2)  |
| 12 months                         | 73.1 (59.8 to 82.6)  | 69.5 (59.5 to 77.5)  | 83.8 (72.0 to 91.0)  | 74.9 (67.5 to 80.9)  |
| 24 months                         | 53.3 (39.6 to 65.2)  | 50.6 (40.3 to 60.0)  | 66.8 (53.3 to 77.2)  | 56.8 (48.7 to 64.1)  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Safety and tolerability of Nivolumab, Ipilimumab and Nivolumab in combination with Ipilimumab as measured by SAEs and AEs leading to discontinuation of study drug

|                 |  |
|-----------------|--|
| End point title | Safety and tolerability of Nivolumab, Ipilimumab and Nivolumab in combination with Ipilimumab as measured by SAEs and AEs leading to discontinuation of study drug <sup>[17]</sup> |
|-----------------|--|

End point description:

The assessment of safety was based on frequency of serious adverse events (SAEs) and AEs leading to discontinuation of study drug. AEs were graded for severity according to the NCI CTCAE version 4.0.

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

End point timeframe:

From enrollment to 100 days after the last dose date (up to approximately 2 years)

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: All participants listed in the baseline period who received treatment per the protocol are reported in the subject analysis sets which are subsets of the full population.

| End point values               | N3 60M Prog     | N3 30M BM       | N1 60M + I3 90M      | N3 60M Naive         |
|--------------------------------|-----------------|-----------------|----------------------|----------------------|
| Subject group type             | Reporting group | Reporting group | Subject analysis set | Subject analysis set |
| Number of subjects analysed    | 44              | 10              | 27                   | 41                   |
| Units: Events                  |                 |                 |                      |                      |
| SAEs                           | 22              | 4               | 20                   | 20                   |
| AEs Leading to Discontinuation | 6               | 2               | 12                   | 2                    |

| <b>End point values</b>        | N1 30M + I3<br>30M Non-BM | N3 30M Non-<br>BM    | N1 30M I3 30M<br>BM  |  |
|--------------------------------|---------------------------|----------------------|----------------------|--|
| Subject group type             | Subject analysis set      | Subject analysis set | Subject analysis set |  |
| Number of subjects analysed    | 25                        | 11                   | 10                   |  |
| Units: Events                  |                           |                      |                      |  |
| SAEs                           | 14                        | 2                    | 7                    |  |
| AEs Leading to Discontinuation | 9                         | 1                    | 4                    |  |

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

From first dose up to 100 days after last dose of study drug, approximately 75 months

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

### Dictionary used

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

|                    |            |
|--------------------|------------|
| Dictionary version | MedDRA21.1 |
|--------------------|------------|

### Reporting groups

|                       |              |
|-----------------------|--------------|
| Reporting group title | N3 60M NAIVE |
|-----------------------|--------------|

Reporting group description:

Treatment Group: N3 = Nivolumab 3mg/kg; 60M = 60 minute infusion; Naive = Anti-CTLA4 Naive

|                       |                     |
|-----------------------|---------------------|
| Reporting group title | N1 60M + I3 90M, W2 |
|-----------------------|---------------------|

Reporting group description:

Treatment Group: N1 = Nivolumab 1mg/kg; I3 = Ipilimumab 3 mg/kg; 90M = 90 minute infusion; 60M = 60 minute infusion; W2 = Week 2 Biopsy

|                       |                     |
|-----------------------|---------------------|
| Reporting group title | N1 60M + I3 90M, W4 |
|-----------------------|---------------------|

Reporting group description:

Treatment Group: N1 = Nivolumab 1mg/kg; I3 = Ipilimumab 3 mg/kg; 90M = 90 minute infusion; 60M = 60 minute infusion; W4 = Week 4 Biopsy

|                       |                     |
|-----------------------|---------------------|
| Reporting group title | N1 60M + I3 90M, WU |
|-----------------------|---------------------|

Reporting group description:

Treatment Group: N1 = Nivolumab 1mg/kg; I3 = Ipilimumab 3 mg/kg; 90M = 90 minute infusion; 60M = 60 minute infusion; WU = Unknown Week Biopsy

|                       |             |
|-----------------------|-------------|
| Reporting group title | N3 60M PROG |
|-----------------------|-------------|

Reporting group description:

Treatment Group: N3 = Nivolumab 3mg/kg; 60M = 60 minute infusion; PROG = Anti-CTLA4 Progressed

|                       |                        |
|-----------------------|------------------------|
| Reporting group title | N1 30M + I3 30M non-BM |
|-----------------------|------------------------|

Reporting group description:

Treatment Group: N1 = Nivolumab 1mg/kg; I3 = Ipilimumab 3 mg/kg; 30M = 30 minute infusion; BM = Brain metastases

|                       |                    |
|-----------------------|--------------------|
| Reporting group title | N1 30M + I3 30M BM |
|-----------------------|--------------------|

Reporting group description:

Treatment Group: N1 = Nivolumab 1mg/kg; I3 = Ipilimumab 3 mg/kg; 30M = 30 minute infusion; BM = Brain metastases

|                       |               |
|-----------------------|---------------|
| Reporting group title | N3 30M non-BM |
|-----------------------|---------------|

Reporting group description:

Treatment Group: N3 = Nivolumab 3mg/kg; 30M = 30 minute infusion; BM = Brain metastases

|                       |                |
|-----------------------|----------------|
| Reporting group title | I3 Monotherapy |
|-----------------------|----------------|

Reporting group description:

Treatment Group: I3 = Ipilimumab 3 mg/kg infusion. Participant was enrolled prior to the closure of this arm via amendment

|                       |           |
|-----------------------|-----------|
| Reporting group title | N3 30M BM |
|-----------------------|-----------|

Reporting group description:

Treatment Group: N3 = Nivolumab 3mg/kg; 30M = 30 minute infusion; BM = Brain metastases

|                       |                     |
|-----------------------|---------------------|
| Reporting group title | Unplanned Treatment |
|-----------------------|---------------------|

Reporting group description:

Treatment Group: Unplanned treatment of Nivolumab 1 mg/kg x 4 then Nivolumab 3 mg/kg

| <b>Serious adverse events</b>                                       | <b>N3 60M NAIVE</b> | <b>N1 60M + I3 90M,<br/>W2</b> | <b>N1 60M + I3 90M,<br/>W4</b> |
|---|---------------------|--------------------------------|--------------------------------|
| Total subjects affected by serious adverse events                   |                     |                                |                                |
| subjects affected / exposed   | 20 / 41 (48.78%)    | 8 / 11 (72.73%)                | 6 / 10 (60.00%)                |
| number of deaths (all causes)                                       | 26                  | 4                              | 3                              |
| number of deaths resulting from adverse events                      |                     |                                |                                |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                     |                                |                                |
| Basal cell carcinoma  |                     |                                |                                |
| subjects affected / exposed   | 0 / 41 (0.00%)      | 0 / 11 (0.00%)                 | 0 / 10 (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   | 3 / 41 (7.32%)      | 0 / 11 (0.00%)                 | 2 / 10 (20.00%)                |
| occurrences causally related to treatment / all                     | 0 / 3               | 0 / 0                          | 0 / 2                          |
| deaths causally related to treatment / all                          | 0 / 2               | 0 / 0                          | 0 / 2                          |
| Metastases to central nervous system                                |                     |                                |                                |
| subjects affected / exposed   | 0 / 41 (0.00%)      | 0 / 11 (0.00%)                 | 1 / 10 (10.00%)                |
| occurrences causally related to treatment / all                     | 0 / 0               | 0 / 0                          | 0 / 1                          |
| deaths causally related to treatment / all                          | 0 / 0               | 0 / 0                          | 0 / 0                          |
| Metastatic neoplasm   |                     |                                |                                |
| subjects affected / exposed   | 0 / 41 (0.00%)      | 0 / 11 (0.00%)                 | 0 / 10 (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   |                     |                                |                                |
| subjects affected / exposed   | 0 / 41 (0.00%)      | 0 / 11 (0.00%)                 | 0 / 10 (0.00%)                 |
| occurrences causally related to treatment / all                     | 0 / 0               | 0 / 0                          | 0 / 0                          |
| deaths causally related to treatment / all                          | 0 / 0               | 0 / 0                          | 0 / 0                          |
| Tumour pain   |                     |                                |                                |
| subjects affected / exposed   | 0 / 41 (0.00%)      | 0 / 11 (0.00%)                 | 0 / 10 (0.00%)                 |
| occurrences causally related to treatment / all                     | 0 / 0               | 0 / 0                          | 0 / 0                          |
| deaths causally related to treatment / all                          | 0 / 0               | 0 / 0                          | 0 / 0                          |
| Vascular disorders  |                     |                                |                                |
| Hypotension   |                     |                                |                                |

|  |                |                |                 |
|--|----------------|----------------|-----------------|
| subjects affected / exposed                          | 0 / 41 (0.00%) | 1 / 11 (9.09%) | 0 / 10 (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 |                |                |                 |
| Fatigue  |                |                |                 |
| subjects affected / exposed                          | 1 / 41 (2.44%) | 0 / 11 (0.00%) | 0 / 10 (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                          | 0 / 41 (0.00%) | 0 / 11 (0.00%) | 0 / 10 (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                          | 1 / 41 (2.44%) | 0 / 11 (0.00%) | 0 / 10 (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           |
| Pain   |                |                |                 |
| subjects affected / exposed                          | 0 / 41 (0.00%) | 0 / 11 (0.00%) | 0 / 10 (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                          | 1 / 41 (2.44%) | 1 / 11 (9.09%) | 1 / 10 (10.00%) |
| occurrences causally related to treatment / all      | 1 / 1          | 1 / 1          | 1 / 1           |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0           |
| Immune system disorders                              |                |                |                 |
| Hypersensitivity                                     |                |                |                 |
| subjects affected / exposed                          | 0 / 41 (0.00%) | 0 / 11 (0.00%) | 0 / 10 (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             |                |                |                 |
| Pelvic pain  |                |                |                 |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 1 / 41 (2.44%) | 0 / 11 (0.00%) | 0 / 10 (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          |
| Respiratory, thoracic and mediastinal disorders |                |                |                |
| Acute respiratory failure                       |                |                |                |
| subjects affected / exposed                     | 0 / 41 (0.00%) | 0 / 11 (0.00%) | 0 / 10 (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 / 41 (0.00%) | 0 / 11 (0.00%) | 0 / 10 (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          |
| Pneumonitis                                     |                |                |                |
| subjects affected / exposed                     | 1 / 41 (2.44%) | 1 / 11 (9.09%) | 0 / 10 (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          |
| Pneumothorax                                    |                |                |                |
| subjects affected / exposed                     | 0 / 41 (0.00%) | 0 / 11 (0.00%) | 0 / 10 (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 / 41 (2.44%) | 1 / 11 (9.09%) | 0 / 10 (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          |
| Respiratory failure                             |                |                |                |
| subjects affected / exposed                     | 1 / 41 (2.44%) | 0 / 11 (0.00%) | 0 / 10 (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          |
| Hypoxia   |                |                |                |
| subjects affected / exposed                     | 0 / 41 (0.00%) | 0 / 11 (0.00%) | 0 / 10 (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                           |                |                |                |

|   |                |                |                |
|---|----------------|----------------|----------------|
| Confusional state                               |                |                |                |
| subjects affected / exposed                     | 0 / 41 (0.00%) | 0 / 11 (0.00%) | 0 / 10 (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          |
| Mental status changes                           |                |                |                |
| subjects affected / exposed                     | 0 / 41 (0.00%) | 0 / 11 (0.00%) | 0 / 10 (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          |
| Investigations                                  |                |                |                |
| Alanine aminotransferase increased              |                |                |                |
| subjects affected / exposed                     | 2 / 41 (4.88%) | 0 / 11 (0.00%) | 0 / 10 (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          |
| Aspartate aminotransferase increased            |                |                |                |
| subjects affected / exposed                     | 1 / 41 (2.44%) | 0 / 11 (0.00%) | 0 / 10 (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 alkaline phosphatase increased            |                |                |                |
| subjects affected / exposed                     | 1 / 41 (2.44%) | 0 / 11 (0.00%) | 0 / 10 (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 bilirubin increased                       |                |                |                |
| subjects affected / exposed                     | 0 / 41 (0.00%) | 0 / 11 (0.00%) | 0 / 10 (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 enzyme increased                        |                |                |                |
| subjects affected / exposed                     | 0 / 41 (0.00%) | 0 / 11 (0.00%) | 0 / 10 (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 / 41 (0.00%) | 0 / 11 (0.00%) | 0 / 10 (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  |                |                |                 |
| Brain herniation                                |                |                |                 |
| subjects affected / exposed                     | 0 / 41 (0.00%) | 0 / 11 (0.00%) | 0 / 10 (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 limb fracture                             |                |                |                 |
| subjects affected / exposed                     | 0 / 41 (0.00%) | 0 / 11 (0.00%) | 0 / 10 (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           |
| Fall  |                |                |                 |
| subjects affected / exposed                     | 0 / 41 (0.00%) | 0 / 11 (0.00%) | 0 / 10 (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 myocardial infarction                     |                |                |                 |
| subjects affected / exposed                     | 0 / 41 (0.00%) | 0 / 11 (0.00%) | 0 / 10 (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                     | 0 / 41 (0.00%) | 0 / 11 (0.00%) | 1 / 10 (10.00%) |
| 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 failure                                 |                |                |                 |
| subjects affected / exposed                     | 0 / 41 (0.00%) | 0 / 11 (0.00%) | 0 / 10 (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 congestive                      |                |                |                 |
| subjects affected / exposed                     | 0 / 41 (0.00%) | 0 / 11 (0.00%) | 1 / 10 (10.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Myocardial infarction                           |                |                |                 |
| subjects affected / exposed                     | 0 / 41 (0.00%) | 0 / 11 (0.00%) | 0 / 10 (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                        |                |                |                 |
| Aphasia   |                |                |                 |
| subjects affected / exposed                     | 0 / 41 (0.00%) | 0 / 11 (0.00%) | 0 / 10 (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           |
| Arachnoiditis                                   |                |                |                 |
| subjects affected / exposed                     | 0 / 41 (0.00%) | 0 / 11 (0.00%) | 0 / 10 (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 / 41 (0.00%) | 0 / 11 (0.00%) | 0 / 10 (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           |
| Dysaesthesia                                    |                |                |                 |
| subjects affected / exposed                     | 0 / 41 (0.00%) | 0 / 11 (0.00%) | 0 / 10 (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                     | 0 / 41 (0.00%) | 1 / 11 (9.09%) | 0 / 10 (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           |
| Hemiparesis                                     |                |                |                 |
| subjects affected / exposed                     | 0 / 41 (0.00%) | 0 / 11 (0.00%) | 0 / 10 (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           |
| Monoplegia                                      |                |                |                 |
| subjects affected / exposed                     | 0 / 41 (0.00%) | 0 / 11 (0.00%) | 1 / 10 (10.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 1           |
| Nervous system disorder                         |                |                |                 |
| subjects affected / exposed                     | 0 / 41 (0.00%) | 0 / 11 (0.00%) | 0 / 10 (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           |
| Nystagmus                                       |                |                |                 |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 41 (0.00%) | 0 / 11 (0.00%) | 0 / 10 (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          |
| Paraesthesia                                    |                |                |                |
| subjects affected / exposed                     | 0 / 41 (0.00%) | 0 / 11 (0.00%) | 0 / 10 (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 / 41 (0.00%) | 0 / 11 (0.00%) | 0 / 10 (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            |                |                |                |
| Anaemia   |                |                |                |
| subjects affected / exposed                     | 0 / 41 (0.00%) | 0 / 11 (0.00%) | 0 / 10 (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 haemolytic anaemia                   |                |                |                |
| subjects affected / exposed                     | 0 / 41 (0.00%) | 0 / 11 (0.00%) | 0 / 10 (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 thrombocytopenic purpura                 |                |                |                |
| subjects affected / exposed                     | 0 / 41 (0.00%) | 0 / 11 (0.00%) | 0 / 10 (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          |
| Thrombocytopenia                                |                |                |                |
| subjects affected / exposed                     | 1 / 41 (2.44%) | 0 / 11 (0.00%) | 0 / 10 (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                                   |                |                |                |
| Iridocyclitis                                   |                |                |                |
| subjects affected / exposed                     | 1 / 41 (2.44%) | 0 / 11 (0.00%) | 0 / 10 (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 pain                                  |                |                 |                 |
| subjects affected / exposed                     | 0 / 41 (0.00%) | 0 / 11 (0.00%)  | 0 / 10 (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 colitis                              |                |                 |                 |
| subjects affected / exposed                     | 0 / 41 (0.00%) | 0 / 11 (0.00%)  | 0 / 10 (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                     | 3 / 41 (7.32%) | 1 / 11 (9.09%)  | 0 / 10 (0.00%)  |
| occurrences causally related to treatment / all | 3 / 3          | 1 / 1           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0           |
| Constipation                                    |                |                 |                 |
| subjects affected / exposed                     | 0 / 41 (0.00%) | 0 / 11 (0.00%)  | 1 / 10 (10.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0           |
| Diarrhoea                                       |                |                 |                 |
| subjects affected / exposed                     | 0 / 41 (0.00%) | 2 / 11 (18.18%) | 0 / 10 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0          | 2 / 2           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0           |
| Enterocolitis                                   |                |                 |                 |
| subjects affected / exposed                     | 0 / 41 (0.00%) | 0 / 11 (0.00%)  | 1 / 10 (10.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           | 1 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0           |
| Intestinal ischaemia                            |                |                 |                 |
| subjects affected / exposed                     | 0 / 41 (0.00%) | 0 / 11 (0.00%)  | 0 / 10 (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           |
| Intra-abdominal fluid collection                |                |                 |                 |
| subjects affected / exposed                     | 0 / 41 (0.00%) | 0 / 11 (0.00%)  | 0 / 10 (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           |
| Necrotising oesophagitis                        |                |                 |                 |

|   |                |                |                 |
|---|----------------|----------------|-----------------|
| subjects affected / exposed                     | 0 / 41 (0.00%) | 0 / 11 (0.00%) | 0 / 10 (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           |
| Pancreatitis                                    |                |                |                 |
| subjects affected / exposed                     | 0 / 41 (0.00%) | 0 / 11 (0.00%) | 0 / 10 (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                     | 1 / 41 (2.44%) | 0 / 11 (0.00%) | 0 / 10 (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           |
| Volvulus  |                |                |                 |
| subjects affected / exposed                     | 0 / 41 (0.00%) | 0 / 11 (0.00%) | 0 / 10 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Vomiting  |                |                |                 |
| subjects affected / exposed                     | 1 / 41 (2.44%) | 0 / 11 (0.00%) | 1 / 10 (10.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Nausea  |                |                |                 |
| subjects affected / exposed                     | 0 / 41 (0.00%) | 0 / 11 (0.00%) | 0 / 10 (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 hepatitis                            |                |                |                 |
| subjects affected / exposed                     | 0 / 41 (0.00%) | 0 / 11 (0.00%) | 0 / 10 (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 obstruction                           |                |                |                 |
| subjects affected / exposed                     | 0 / 41 (0.00%) | 0 / 11 (0.00%) | 1 / 10 (10.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 3           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Hepatitis                                       |                |                |                 |

|   |                |                |                 |
|---|----------------|----------------|-----------------|
| subjects affected / exposed                           | 0 / 41 (0.00%) | 0 / 11 (0.00%) | 0 / 10 (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 / 41 (0.00%) | 1 / 11 (9.09%) | 0 / 10 (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           |
| Immune-mediated hepatitis                             |                |                |                 |
| subjects affected / exposed                           | 0 / 41 (0.00%) | 0 / 11 (0.00%) | 0 / 10 (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           |
| Liver disorder  |                |                |                 |
| subjects affected / exposed                           | 0 / 41 (0.00%) | 0 / 11 (0.00%) | 0 / 10 (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                |                |                |                 |
| Drug reaction with eosinophilia and systemic symptoms |                |                |                 |
| subjects affected / exposed                           | 1 / 41 (2.44%) | 0 / 11 (0.00%) | 0 / 10 (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  |                |                |                 |
| subjects affected / exposed                           | 0 / 41 (0.00%) | 0 / 11 (0.00%) | 1 / 10 (10.00%) |
| occurrences causally related to treatment / all       | 0 / 0          | 0 / 0          | 1 / 1           |
| deaths causally related to treatment / all            | 0 / 0          | 0 / 0          | 0 / 0           |
| Renal and urinary disorders                           |                |                |                 |
| Acute kidney injury                                   |                |                |                 |
| subjects affected / exposed                           | 1 / 41 (2.44%) | 0 / 11 (0.00%) | 0 / 10 (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           |
| Haematuria  |                |                |                 |
| subjects affected / exposed                           | 1 / 41 (2.44%) | 0 / 11 (0.00%) | 0 / 10 (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 / 41 (0.00%) | 0 / 11 (0.00%) | 0 / 10 (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                     | 0 / 41 (0.00%) | 0 / 11 (0.00%) | 0 / 10 (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 / 41 (0.00%) | 0 / 11 (0.00%) | 0 / 10 (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 / 41 (0.00%) | 0 / 11 (0.00%) | 0 / 10 (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 |                |                |                |
| Arthritis                                       |                |                |                |
| subjects affected / exposed                     | 0 / 41 (0.00%) | 0 / 11 (0.00%) | 0 / 10 (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 / 41 (2.44%) | 0 / 11 (0.00%) | 0 / 10 (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          |
| Bone disorder                                   |                |                |                |
| subjects affected / exposed                     | 0 / 41 (0.00%) | 0 / 11 (0.00%) | 0 / 10 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Flank pain                                      |                |                |                |
| subjects affected / exposed                     | 1 / 41 (2.44%) | 0 / 11 (0.00%) | 0 / 10 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |

|   |                |                |                |
|---|----------------|----------------|----------------|
| Musculoskeletal chest pain                      |                |                |                |
| subjects affected / exposed                     | 1 / 41 (2.44%) | 0 / 11 (0.00%) | 0 / 10 (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          |
| Pain in extremity                               |                |                |                |
| subjects affected / exposed                     | 0 / 41 (0.00%) | 0 / 11 (0.00%) | 0 / 10 (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                     |                |                |                |
| Clostridium difficile infection                 |                |                |                |
| subjects affected / exposed                     | 0 / 41 (0.00%) | 0 / 11 (0.00%) | 0 / 10 (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                     | 0 / 41 (0.00%) | 0 / 11 (0.00%) | 0 / 10 (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          |
| Liver abscess                                   |                |                |                |
| subjects affected / exposed                     | 0 / 41 (0.00%) | 0 / 11 (0.00%) | 0 / 10 (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 / 41 (0.00%) | 0 / 11 (0.00%) | 0 / 10 (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                     | 0 / 41 (0.00%) | 0 / 11 (0.00%) | 0 / 10 (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                     | 1 / 41 (2.44%) | 0 / 11 (0.00%) | 0 / 10 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Sepsis  |                |                |                |

|   |                |                |                 |
|---|----------------|----------------|-----------------|
| subjects affected / exposed                     | 0 / 41 (0.00%) | 0 / 11 (0.00%) | 0 / 10 (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 / 41 (0.00%) | 0 / 11 (0.00%) | 0 / 10 (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           |
| Staphylococcal infection                        |                |                |                 |
| subjects affected / exposed                     | 1 / 41 (2.44%) | 0 / 11 (0.00%) | 0 / 10 (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 infection                         |                |                |                 |
| subjects affected / exposed                     | 0 / 41 (0.00%) | 0 / 11 (0.00%) | 0 / 10 (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           |
| Metabolism and nutrition disorders              |                |                |                 |
| Dehydration                                     |                |                |                 |
| subjects affected / exposed                     | 1 / 41 (2.44%) | 0 / 11 (0.00%) | 0 / 10 (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           |
| Failure to thrive                               |                |                |                 |
| subjects affected / exposed                     | 0 / 41 (0.00%) | 1 / 11 (9.09%) | 1 / 10 (10.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 3          | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Hyperglycaemia                                  |                |                |                 |
| subjects affected / exposed                     | 0 / 41 (0.00%) | 0 / 11 (0.00%) | 0 / 10 (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                     | 1 / 41 (2.44%) | 0 / 11 (0.00%) | 0 / 10 (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           |
| Hypokalaemia                                    |                |                |                 |



|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 41 (0.00%) | 0 / 11 (0.00%) | 0 / 10 (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                     | 1 / 41 (2.44%) | 1 / 11 (9.09%) | 0 / 10 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 1 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |

| <b>Serious adverse events</b>                                       | N1 60M + I3 90M, WU | N3 60M PROG      | N1 30M + I3 30M non-BM |
|---|---------------------|------------------|------------------------|
| Total subjects affected by serious adverse events                   |                     |                  |                        |
| subjects affected / exposed   | 6 / 6 (100.00%)     | 22 / 44 (50.00%) | 14 / 25 (56.00%)       |
| number of deaths (all causes)                                       | 4                   | 25               | 14                     |
| number of deaths resulting from adverse events                      |                     |                  |                        |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                     |                  |                        |
| Basal cell carcinoma  |                     |                  |                        |
| subjects affected / exposed   | 0 / 6 (0.00%)       | 1 / 44 (2.27%)   | 0 / 25 (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                  |
| Malignant neoplasm progression                                      |                     |                  |                        |
| subjects affected / exposed   | 3 / 6 (50.00%)      | 8 / 44 (18.18%)  | 4 / 25 (16.00%)        |
| occurrences causally related to treatment / all                     | 0 / 3               | 0 / 8            | 0 / 4                  |
| deaths causally related to treatment / all                          | 0 / 3               | 0 / 7            | 0 / 1                  |
| Metastases to central nervous system                                |                     |                  |                        |
| subjects affected / exposed   | 0 / 6 (0.00%)       | 0 / 44 (0.00%)   | 0 / 25 (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                  |
| Metastatic neoplasm   |                     |                  |                        |
| subjects affected / exposed   | 0 / 6 (0.00%)       | 1 / 44 (2.27%)   | 0 / 25 (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                  |
| Squamous cell carcinoma   |                     |                  |                        |

|  |                |                |                 |
|--|----------------|----------------|-----------------|
| subjects affected / exposed                          | 0 / 6 (0.00%)  | 1 / 44 (2.27%) | 0 / 25 (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 pain  |                |                |                 |
| subjects affected / exposed                          | 0 / 6 (0.00%)  | 0 / 44 (0.00%) | 0 / 25 (0.00%)  |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0           |
| Vascular disorders                                   |                |                |                 |
| Hypotension  |                |                |                 |
| subjects affected / exposed                          | 0 / 6 (0.00%)  | 0 / 44 (0.00%) | 1 / 25 (4.00%)  |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 1           |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0           |
| General disorders and administration site conditions |                |                |                 |
| Fatigue  |                |                |                 |
| subjects affected / exposed                          | 0 / 6 (0.00%)  | 0 / 44 (0.00%) | 0 / 25 (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 / 6 (0.00%)  | 0 / 44 (0.00%) | 0 / 25 (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 / 6 (0.00%)  | 0 / 44 (0.00%) | 0 / 25 (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 / 6 (16.67%) | 0 / 44 (0.00%) | 0 / 25 (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           |
| Pyrexia  |                |                |                 |
| subjects affected / exposed                          | 1 / 6 (16.67%) | 1 / 44 (2.27%) | 3 / 25 (12.00%) |
| occurrences causally related to treatment / all      | 0 / 1          | 0 / 1          | 3 / 3           |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0           |

|   |                |                |                |
|---|----------------|----------------|----------------|
| Immune system disorders                         |                |                |                |
| Hypersensitivity                                |                |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 44 (0.00%) | 0 / 25 (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        |                |                |                |
| Pelvic pain                                     |                |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 44 (0.00%) | 0 / 25 (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 failure                       |                |                |                |
| subjects affected / exposed                     | 1 / 6 (16.67%) | 0 / 44 (0.00%) | 0 / 25 (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          |
| Dyspnoea  |                |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 44 (0.00%) | 1 / 25 (4.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Pneumonitis                                     |                |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 1 / 44 (2.27%) | 0 / 25 (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          |
| Pneumothorax                                    |                |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 44 (0.00%) | 1 / 25 (4.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Pulmonary embolism                              |                |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 44 (0.00%) | 1 / 25 (4.00%) |
| 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 failure                             |                |                |                |

|   |               |                |                |
|---|---------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 44 (0.00%) | 0 / 25 (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          |
| Hypoxia   |               |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 44 (0.00%) | 0 / 25 (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                           |               |                |                |
| Confusional state                               |               |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 44 (0.00%) | 0 / 25 (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          |
| Mental status changes                           |               |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 44 (0.00%) | 0 / 25 (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          |
| Investigations                                  |               |                |                |
| Alanine aminotransferase increased              |               |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 44 (0.00%) | 0 / 25 (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 / 6 (0.00%) | 0 / 44 (0.00%) | 0 / 25 (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 alkaline phosphatase increased            |               |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 44 (0.00%) | 0 / 25 (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 bilirubin increased                       |               |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 44 (0.00%) | 0 / 25 (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 enzyme increased                        |                |                |                |
| subjects affected / exposed                     | 1 / 6 (16.67%) | 0 / 44 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 1 / 1          | 0 / 0          | 0 / 0          |
| Lipase increased                                |                |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 1 / 44 (2.27%) | 0 / 25 (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          |
| Injury, poisoning and procedural complications  |                |                |                |
| Brain herniation                                |                |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 1 / 44 (2.27%) | 0 / 25 (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          |
| Lower limb fracture                             |                |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 44 (0.00%) | 1 / 25 (4.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Fall  |                |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 44 (0.00%) | 0 / 25 (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 myocardial infarction                     |                |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 1 / 44 (2.27%) | 0 / 25 (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          |
| Atrial fibrillation                             |                |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 44 (0.00%) | 0 / 25 (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 / 6 (0.00%)  | 1 / 44 (2.27%) | 0 / 25 (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          |

|   |                |                |                |
|---|----------------|----------------|----------------|
| Cardiac failure congestive                      |                |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 1 / 44 (2.27%) | 0 / 25 (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          |
| Myocardial infarction                           |                |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 1 / 44 (2.27%) | 1 / 25 (4.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 1          | 0 / 0          |
| Nervous system disorders                        |                |                |                |
| Aphasia   |                |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 44 (0.00%) | 0 / 25 (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          |
| Arachnoiditis                                   |                |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 44 (0.00%) | 1 / 25 (4.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 1 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Dizziness                                       |                |                |                |
| subjects affected / exposed                     | 1 / 6 (16.67%) | 0 / 44 (0.00%) | 0 / 25 (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          |
| Dysaesthesia                                    |                |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 44 (0.00%) | 0 / 25 (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                     | 0 / 6 (0.00%)  | 0 / 44 (0.00%) | 0 / 25 (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          |
| Hemiparesis                                     |                |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 44 (0.00%) | 0 / 25 (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          |
| Monoplegia                                      |                |                |                |

|   |               |                |                |
|---|---------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 44 (0.00%) | 0 / 25 (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 disorder                         |               |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 44 (0.00%) | 0 / 25 (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          |
| Nystagmus                                       |               |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 44 (0.00%) | 0 / 25 (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          |
| Paraesthesia                                    |               |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 44 (0.00%) | 0 / 25 (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 / 6 (0.00%) | 0 / 44 (0.00%) | 0 / 25 (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            |               |                |                |
| Anaemia   |               |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 1 / 44 (2.27%) | 0 / 25 (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          |
| Autoimmune haemolytic anaemia                   |               |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 44 (0.00%) | 0 / 25 (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 thrombocytopenic purpura                 |               |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 44 (0.00%) | 0 / 25 (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          |
| Thrombocytopenia                                |               |                |                |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 44 (0.00%) | 0 / 25 (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                                   |                |                |                |
| Iridocyclitis                                   |                |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 44 (0.00%) | 0 / 25 (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 pain                                  |                |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 1 / 44 (2.27%) | 1 / 25 (4.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          | 1 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Autoimmune colitis                              |                |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 44 (0.00%) | 0 / 25 (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                     | 2 / 6 (33.33%) | 0 / 44 (0.00%) | 2 / 25 (8.00%) |
| occurrences causally related to treatment / all | 2 / 2          | 0 / 0          | 2 / 2          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Constipation                                    |                |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 44 (0.00%) | 0 / 25 (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          |
| Diarrhoea                                       |                |                |                |
| subjects affected / exposed                     | 2 / 6 (33.33%) | 0 / 44 (0.00%) | 1 / 25 (4.00%) |
| occurrences causally related to treatment / all | 2 / 2          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Enterocolitis                                   |                |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 44 (0.00%) | 1 / 25 (4.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 1 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Intestinal ischaemia                            |                |                |                |



|   |               |                |                |
|---|---------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 44 (0.00%) | 0 / 25 (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          |
| Intra-abdominal fluid collection                |               |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 1 / 44 (2.27%) | 0 / 25 (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          |
| Necrotising oesophagitis                        |               |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 44 (0.00%) | 0 / 25 (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          |
| Pancreatitis                                    |               |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 1 / 44 (2.27%) | 1 / 25 (4.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 1          | 1 / 1          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Small intestinal obstruction                    |               |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 44 (0.00%) | 0 / 25 (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          |
| Volvulus  |               |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 1 / 44 (2.27%) | 0 / 25 (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          |
| Vomiting  |               |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 44 (0.00%) | 1 / 25 (4.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 2          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Nausea  |               |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 44 (0.00%) | 0 / 25 (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 hepatitis                            |               |                |                |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                           | 1 / 6 (16.67%) | 0 / 44 (0.00%) | 0 / 25 (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          |
| Bile duct obstruction                                 |                |                |                |
| subjects affected / exposed                           | 0 / 6 (0.00%)  | 0 / 44 (0.00%) | 0 / 25 (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 / 6 (0.00%)  | 0 / 44 (0.00%) | 1 / 25 (4.00%) |
| occurrences causally related to treatment / all       | 0 / 0          | 0 / 0          | 1 / 1          |
| deaths causally related to treatment / all            | 0 / 0          | 0 / 0          | 0 / 0          |
| Hepatotoxicity  |                |                |                |
| subjects affected / exposed                           | 0 / 6 (0.00%)  | 0 / 44 (0.00%) | 0 / 25 (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 hepatitis                             |                |                |                |
| subjects affected / exposed                           | 0 / 6 (0.00%)  | 0 / 44 (0.00%) | 1 / 25 (4.00%) |
| occurrences causally related to treatment / all       | 0 / 0          | 0 / 0          | 1 / 1          |
| deaths causally related to treatment / all            | 0 / 0          | 0 / 0          | 0 / 0          |
| Liver disorder  |                |                |                |
| subjects affected / exposed                           | 0 / 6 (0.00%)  | 1 / 44 (2.27%) | 0 / 25 (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          |
| Skin and subcutaneous tissue disorders                |                |                |                |
| Drug reaction with eosinophilia and systemic symptoms |                |                |                |
| subjects affected / exposed                           | 0 / 6 (0.00%)  | 0 / 44 (0.00%) | 0 / 25 (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 / 6 (0.00%)  | 0 / 44 (0.00%) | 0 / 25 (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                           |                |                |                |

|   |               |                |                |
|---|---------------|----------------|----------------|
| Acute kidney injury                             |               |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 1 / 44 (2.27%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Haematuria                                      |               |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 44 (0.00%) | 0 / 25 (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 / 6 (0.00%) | 1 / 44 (2.27%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Endocrine disorders                             |               |                |                |
| Adrenal insufficiency                           |               |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 44 (0.00%) | 0 / 25 (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 / 6 (0.00%) | 0 / 44 (0.00%) | 0 / 25 (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 / 6 (0.00%) | 0 / 44 (0.00%) | 1 / 25 (4.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 1 / 1          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Musculoskeletal and connective tissue disorders |               |                |                |
| Arthritis                                       |               |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 1 / 44 (2.27%) | 0 / 25 (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          |
| Back pain                                       |               |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 44 (0.00%) | 0 / 25 (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          |

|   |                |                |                |
|---|----------------|----------------|----------------|
| Bone disorder                                   |                |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 44 (0.00%) | 1 / 25 (4.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Flank pain                                      |                |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 44 (0.00%) | 0 / 25 (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 chest pain                      |                |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 44 (0.00%) | 0 / 25 (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 in extremity                               |                |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 44 (0.00%) | 0 / 25 (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                     |                |                |                |
| Clostridium difficile infection                 |                |                |                |
| subjects affected / exposed                     | 1 / 6 (16.67%) | 0 / 44 (0.00%) | 0 / 25 (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 / 6 (0.00%)  | 0 / 44 (0.00%) | 1 / 25 (4.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 1 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Liver abscess                                   |                |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 1 / 44 (2.27%) | 0 / 25 (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          |
| Meningitis                                      |                |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 1 / 44 (2.27%) | 1 / 25 (4.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          | 1 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Pneumonia                                       |                |                |                |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 44 (0.00%) | 0 / 25 (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 / 6 (0.00%)  | 0 / 44 (0.00%) | 0 / 25 (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          |
| Sepsis  |                |                |                |
| subjects affected / exposed                     | 1 / 6 (16.67%) | 0 / 44 (0.00%) | 0 / 25 (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          |
| Sinusitis                                       |                |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 1 / 44 (2.27%) | 0 / 25 (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          |
| Staphylococcal infection                        |                |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 44 (0.00%) | 0 / 25 (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                     | 1 / 6 (16.67%) | 1 / 44 (2.27%) | 0 / 25 (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          |
| Metabolism and nutrition disorders              |                |                |                |
| Dehydration                                     |                |                |                |
| subjects affected / exposed                     | 2 / 6 (33.33%) | 0 / 44 (0.00%) | 1 / 25 (4.00%) |
| occurrences causally related to treatment / all | 0 / 2          | 0 / 0          | 1 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Failure to thrive                               |                |                |                |
| subjects affected / exposed                     | 1 / 6 (16.67%) | 0 / 44 (0.00%) | 0 / 25 (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          |
| Hyperglycaemia                                  |                |                |                |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 1 / 44 (2.27%) | 0 / 25 (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          |
| Hyperkalaemia                                   |                |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 44 (0.00%) | 0 / 25 (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                     | 1 / 6 (16.67%) | 0 / 44 (0.00%) | 0 / 25 (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          |
| Hyponatraemia                                   |                |                |                |
| subjects affected / exposed                     | 1 / 6 (16.67%) | 0 / 44 (0.00%) | 0 / 25 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |

| <b>Serious adverse events</b>                                       | N1 30M + I3 30M<br>BM | N3 30M non-BM   | I3 Monotherapy  |
|---|-----------------------|-----------------|-----------------|
| Total subjects affected by serious adverse events                   |                       |                 |                 |
| subjects affected / exposed   | 7 / 10 (70.00%)       | 2 / 11 (18.18%) | 1 / 1 (100.00%) |
| number of deaths (all causes)                                       | 2                     | 4               | 1               |
| number of deaths resulting from adverse events                      |                       |                 |                 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                       |                 |                 |
| Basal cell carcinoma  |                       |                 |                 |
| subjects affected / exposed   | 0 / 10 (0.00%)        | 0 / 11 (0.00%)  | 0 / 1 (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   | 1 / 10 (10.00%)       | 1 / 11 (9.09%)  | 0 / 1 (0.00%)   |
| occurrences causally related to treatment / all                     | 0 / 1                 | 0 / 1           | 0 / 0           |
| deaths causally related to treatment / all                          | 0 / 1                 | 0 / 1           | 0 / 0           |
| Metastases to central nervous system                                |                       |                 |                 |

|  |                 |                |                 |
|--|-----------------|----------------|-----------------|
| subjects affected / exposed                          | 0 / 10 (0.00%)  | 0 / 11 (0.00%) | 0 / 1 (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           |
| Metastatic neoplasm                                  |                 |                |                 |
| subjects affected / exposed                          | 0 / 10 (0.00%)  | 0 / 11 (0.00%) | 0 / 1 (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                              |                 |                |                 |
| subjects affected / exposed                          | 0 / 10 (0.00%)  | 0 / 11 (0.00%) | 0 / 1 (0.00%)   |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0          | 0 / 0           |
| Tumour pain  |                 |                |                 |
| subjects affected / exposed                          | 0 / 10 (0.00%)  | 0 / 11 (0.00%) | 1 / 1 (100.00%) |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 1           |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0          | 0 / 0           |
| Vascular disorders                                   |                 |                |                 |
| Hypotension  |                 |                |                 |
| subjects affected / exposed                          | 0 / 10 (0.00%)  | 0 / 11 (0.00%) | 0 / 1 (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 |                 |                |                 |
| Fatigue  |                 |                |                 |
| subjects affected / exposed                          | 0 / 10 (0.00%)  | 0 / 11 (0.00%) | 0 / 1 (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                          | 1 / 10 (10.00%) | 0 / 11 (0.00%) | 0 / 1 (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           |
| Non-cardiac chest pain                               |                 |                |                 |
| subjects affected / exposed                          | 0 / 10 (0.00%)  | 0 / 11 (0.00%) | 0 / 1 (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                     | 0 / 10 (0.00%)  | 0 / 11 (0.00%) | 0 / 1 (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                     | 0 / 10 (0.00%)  | 0 / 11 (0.00%) | 0 / 1 (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 system disorders                         |                 |                |               |
| Hypersensitivity                                |                 |                |               |
| subjects affected / exposed                     | 1 / 10 (10.00%) | 0 / 11 (0.00%) | 0 / 1 (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        |                 |                |               |
| Pelvic pain                                     |                 |                |               |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 0 / 11 (0.00%) | 0 / 1 (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 failure                       |                 |                |               |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 0 / 11 (0.00%) | 0 / 1 (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 / 10 (0.00%)  | 0 / 11 (0.00%) | 0 / 1 (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         |
| Pneumonitis                                     |                 |                |               |
| subjects affected / exposed                     | 1 / 10 (10.00%) | 0 / 11 (0.00%) | 0 / 1 (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         |
| Pneumothorax                                    |                 |                |               |



|   |                |                |               |
|---|----------------|----------------|---------------|
| subjects affected / exposed                     | 0 / 10 (0.00%) | 0 / 11 (0.00%) | 0 / 1 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Pulmonary embolism                              |                |                |               |
| subjects affected / exposed                     | 0 / 10 (0.00%) | 0 / 11 (0.00%) | 0 / 1 (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 failure                             |                |                |               |
| subjects affected / exposed                     | 0 / 10 (0.00%) | 0 / 11 (0.00%) | 0 / 1 (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         |
| Hypoxia   |                |                |               |
| subjects affected / exposed                     | 0 / 10 (0.00%) | 0 / 11 (0.00%) | 0 / 1 (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                           |                |                |               |
| Confusional state                               |                |                |               |
| subjects affected / exposed                     | 0 / 10 (0.00%) | 0 / 11 (0.00%) | 0 / 1 (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         |
| Mental status changes                           |                |                |               |
| subjects affected / exposed                     | 0 / 10 (0.00%) | 0 / 11 (0.00%) | 0 / 1 (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         |
| Investigations                                  |                |                |               |
| Alanine aminotransferase increased              |                |                |               |
| subjects affected / exposed                     | 0 / 10 (0.00%) | 0 / 11 (0.00%) | 0 / 1 (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 / 10 (0.00%) | 0 / 11 (0.00%) | 0 / 1 (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 alkaline phosphatase increased            |                 |                |               |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 0 / 11 (0.00%) | 0 / 1 (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 bilirubin increased                       |                 |                |               |
| subjects affected / exposed                     | 1 / 10 (10.00%) | 0 / 11 (0.00%) | 0 / 1 (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         |
| Hepatic enzyme increased                        |                 |                |               |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 0 / 11 (0.00%) | 0 / 1 (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 / 10 (0.00%)  | 0 / 11 (0.00%) | 0 / 1 (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  |                 |                |               |
| Brain herniation                                |                 |                |               |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 0 / 11 (0.00%) | 0 / 1 (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 limb fracture                             |                 |                |               |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 0 / 11 (0.00%) | 0 / 1 (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         |
| Fall  |                 |                |               |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 0 / 11 (0.00%) | 0 / 1 (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 myocardial infarction                     |                 |                |               |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 0 / 11 (0.00%) | 0 / 1 (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                     | 0 / 10 (0.00%)  | 0 / 11 (0.00%) | 0 / 1 (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 / 10 (0.00%)  | 0 / 11 (0.00%) | 0 / 1 (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 congestive                      |                 |                |               |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 0 / 11 (0.00%) | 0 / 1 (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 / 10 (0.00%)  | 0 / 11 (0.00%) | 0 / 1 (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                        |                 |                |               |
| Aphasia   |                 |                |               |
| subjects affected / exposed                     | 1 / 10 (10.00%) | 0 / 11 (0.00%) | 0 / 1 (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         |
| Arachnoiditis                                   |                 |                |               |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 0 / 11 (0.00%) | 0 / 1 (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 / 10 (0.00%)  | 0 / 11 (0.00%) | 0 / 1 (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         |
| Dysaesthesia                                    |                 |                |               |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 0 / 11 (0.00%) | 0 / 1 (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                     | 0 / 10 (0.00%)  | 0 / 11 (0.00%) | 0 / 1 (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         |
| Hemiparesis                                     |                 |                |               |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 0 / 11 (0.00%) | 0 / 1 (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         |
| Monoplegia                                      |                 |                |               |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 0 / 11 (0.00%) | 0 / 1 (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 disorder                         |                 |                |               |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 1 / 11 (9.09%) | 0 / 1 (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         |
| Nystagmus                                       |                 |                |               |
| subjects affected / exposed                     | 1 / 10 (10.00%) | 0 / 11 (0.00%) | 0 / 1 (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         |
| Paraesthesia                                    |                 |                |               |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 0 / 11 (0.00%) | 0 / 1 (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 / 10 (0.00%)  | 0 / 11 (0.00%) | 0 / 1 (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            |                 |                |               |
| Anaemia   |                 |                |               |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 0 / 11 (0.00%) | 0 / 1 (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 haemolytic anaemia                   |                 |                |               |

|   |                 |                |               |
|---|-----------------|----------------|---------------|
| subjects affected / exposed                     | 1 / 10 (10.00%) | 0 / 11 (0.00%) | 0 / 1 (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         |
| Immune thrombocytopenic purpura                 |                 |                |               |
| subjects affected / exposed                     | 1 / 10 (10.00%) | 0 / 11 (0.00%) | 0 / 1 (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         |
| Thrombocytopenia                                |                 |                |               |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 0 / 11 (0.00%) | 0 / 1 (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                                   |                 |                |               |
| Iridocyclitis                                   |                 |                |               |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 0 / 11 (0.00%) | 0 / 1 (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 pain                                  |                 |                |               |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 0 / 11 (0.00%) | 0 / 1 (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 colitis                              |                 |                |               |
| subjects affected / exposed                     | 1 / 10 (10.00%) | 0 / 11 (0.00%) | 0 / 1 (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         |
| Colitis   |                 |                |               |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 0 / 11 (0.00%) | 0 / 1 (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         |
| Constipation                                    |                 |                |               |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 0 / 11 (0.00%) | 0 / 1 (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         |
| Diarrhoea                                       |                 |                |               |

|   |                 |                |               |
|---|-----------------|----------------|---------------|
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 0 / 11 (0.00%) | 0 / 1 (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         |
| Enterocolitis                                   |                 |                |               |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 0 / 11 (0.00%) | 0 / 1 (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 ischaemia                            |                 |                |               |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 1 / 11 (9.09%) | 0 / 1 (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         |
| Intra-abdominal fluid collection                |                 |                |               |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 0 / 11 (0.00%) | 0 / 1 (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         |
| Necrotising oesophagitis                        |                 |                |               |
| subjects affected / exposed                     | 1 / 10 (10.00%) | 0 / 11 (0.00%) | 0 / 1 (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         |
| Pancreatitis                                    |                 |                |               |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 0 / 11 (0.00%) | 0 / 1 (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                     | 0 / 10 (0.00%)  | 0 / 11 (0.00%) | 0 / 1 (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         |
| Volvulus  |                 |                |               |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 0 / 11 (0.00%) | 0 / 1 (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                     | 0 / 10 (0.00%)  | 0 / 11 (0.00%) | 0 / 1 (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                     | 0 / 10 (0.00%)  | 0 / 11 (0.00%) | 0 / 1 (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 hepatitis                            |                 |                |               |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 0 / 11 (0.00%) | 0 / 1 (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 obstruction                           |                 |                |               |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 0 / 11 (0.00%) | 0 / 1 (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 / 10 (0.00%)  | 0 / 11 (0.00%) | 0 / 1 (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 / 10 (0.00%)  | 0 / 11 (0.00%) | 0 / 1 (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 hepatitis                       |                 |                |               |
| subjects affected / exposed                     | 1 / 10 (10.00%) | 0 / 11 (0.00%) | 0 / 1 (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         |
| Liver disorder                                  |                 |                |               |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 0 / 11 (0.00%) | 0 / 1 (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          |                 |                |               |

|   |                 |                |               |
|---|-----------------|----------------|---------------|
| Drug reaction with eosinophilia and systemic symptoms |                 |                |               |
| subjects affected / exposed                           | 0 / 10 (0.00%)  | 0 / 11 (0.00%) | 0 / 1 (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 / 10 (0.00%)  | 0 / 11 (0.00%) | 0 / 1 (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                           |                 |                |               |
| Acute kidney injury                                   |                 |                |               |
| subjects affected / exposed                           | 1 / 10 (10.00%) | 0 / 11 (0.00%) | 0 / 1 (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         |
| Haematuria  |                 |                |               |
| subjects affected / exposed                           | 0 / 10 (0.00%)  | 0 / 11 (0.00%) | 0 / 1 (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 / 10 (0.00%)  | 0 / 11 (0.00%) | 0 / 1 (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 / 10 (10.00%) | 0 / 11 (0.00%) | 0 / 1 (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         |
| Hyperthyroidism                                       |                 |                |               |
| subjects affected / exposed                           | 1 / 10 (10.00%) | 0 / 11 (0.00%) | 0 / 1 (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         |
| Hypophysitis  |                 |                |               |
| subjects affected / exposed                           | 0 / 10 (0.00%)  | 0 / 11 (0.00%) | 0 / 1 (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 |                |                |               |
| Arthritis                                       |                |                |               |
| subjects affected / exposed                     | 0 / 10 (0.00%) | 0 / 11 (0.00%) | 0 / 1 (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                     | 0 / 10 (0.00%) | 0 / 11 (0.00%) | 0 / 1 (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         |
| Bone disorder                                   |                |                |               |
| subjects affected / exposed                     | 0 / 10 (0.00%) | 0 / 11 (0.00%) | 0 / 1 (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 / 10 (0.00%) | 0 / 11 (0.00%) | 0 / 1 (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 chest pain                      |                |                |               |
| subjects affected / exposed                     | 0 / 10 (0.00%) | 0 / 11 (0.00%) | 0 / 1 (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 in extremity                               |                |                |               |
| subjects affected / exposed                     | 0 / 10 (0.00%) | 0 / 11 (0.00%) | 0 / 1 (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                     |                |                |               |
| Clostridium difficile infection                 |                |                |               |
| subjects affected / exposed                     | 0 / 10 (0.00%) | 0 / 11 (0.00%) | 0 / 1 (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                     | 0 / 10 (0.00%) | 0 / 11 (0.00%) | 0 / 1 (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         |

|   |                 |                |               |
|---|-----------------|----------------|---------------|
| Liver abscess                                   |                 |                |               |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 0 / 11 (0.00%) | 0 / 1 (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 / 10 (0.00%)  | 0 / 11 (0.00%) | 0 / 1 (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 / 10 (10.00%) | 0 / 11 (0.00%) | 0 / 1 (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         |
| Respiratory tract infection                     |                 |                |               |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 0 / 11 (0.00%) | 0 / 1 (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         |
| Sepsis  |                 |                |               |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 0 / 11 (0.00%) | 0 / 1 (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 / 10 (0.00%)  | 0 / 11 (0.00%) | 0 / 1 (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         |
| Staphylococcal infection                        |                 |                |               |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 0 / 11 (0.00%) | 0 / 1 (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                     | 0 / 10 (0.00%)  | 0 / 11 (0.00%) | 0 / 1 (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         |
| Metabolism and nutrition disorders              |                 |                |               |

|   |                |                |               |
|---|----------------|----------------|---------------|
| Dehydration                                     |                |                |               |
| subjects affected / exposed                     | 0 / 10 (0.00%) | 0 / 11 (0.00%) | 0 / 1 (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         |
| Failure to thrive                               |                |                |               |
| subjects affected / exposed                     | 0 / 10 (0.00%) | 0 / 11 (0.00%) | 0 / 1 (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         |
| Hyperglycaemia                                  |                |                |               |
| subjects affected / exposed                     | 0 / 10 (0.00%) | 0 / 11 (0.00%) | 0 / 1 (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 / 10 (0.00%) | 0 / 11 (0.00%) | 0 / 1 (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 / 10 (0.00%) | 0 / 11 (0.00%) | 0 / 1 (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 / 10 (0.00%) | 0 / 11 (0.00%) | 0 / 1 (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         |

| Serious adverse events  | N3 30M BM       | Unplanned Treatment |  |
|---|-----------------|---------------------|--|
| Total subjects affected by serious adverse events                   |                 |                     |  |
| subjects affected / exposed   | 4 / 10 (40.00%) | 1 / 1 (100.00%)     |  |
| number of deaths (all causes)                                       | 4               | 1                   |  |
| number of deaths resulting from adverse events                      |                 |                     |  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                 |                     |  |
| Basal cell carcinoma  |                 |                     |  |

|  |                 |                 |  |
|--|-----------------|-----------------|--|
| subjects affected / exposed                          | 0 / 10 (0.00%)  | 0 / 1 (0.00%)   |  |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           |  |
| Malignant neoplasm progression                       |                 |                 |  |
| subjects affected / exposed                          | 2 / 10 (20.00%) | 1 / 1 (100.00%) |  |
| occurrences causally related to treatment / all      | 0 / 2           | 0 / 1           |  |
| deaths causally related to treatment / all           | 0 / 2           | 0 / 1           |  |
| Metastases to central nervous system                 |                 |                 |  |
| subjects affected / exposed                          | 0 / 10 (0.00%)  | 0 / 1 (0.00%)   |  |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           |  |
| Metastatic neoplasm                                  |                 |                 |  |
| subjects affected / exposed                          | 0 / 10 (0.00%)  | 0 / 1 (0.00%)   |  |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           |  |
| Squamous cell carcinoma                              |                 |                 |  |
| subjects affected / exposed                          | 0 / 10 (0.00%)  | 0 / 1 (0.00%)   |  |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           |  |
| Tumour pain  |                 |                 |  |
| subjects affected / exposed                          | 0 / 10 (0.00%)  | 0 / 1 (0.00%)   |  |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           |  |
| Vascular disorders                                   |                 |                 |  |
| Hypotension  |                 |                 |  |
| subjects affected / exposed                          | 0 / 10 (0.00%)  | 0 / 1 (0.00%)   |  |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           |  |
| General disorders and administration site conditions |                 |                 |  |
| Fatigue  |                 |                 |  |
| subjects affected / exposed                          | 0 / 10 (0.00%)  | 0 / 1 (0.00%)   |  |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 0           |  |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           |  |

|   |                |               |  |
|---|----------------|---------------|--|
| Malaise   |                |               |  |
| subjects affected / exposed                     | 0 / 10 (0.00%) | 0 / 1 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         |  |
| Non-cardiac chest pain                          |                |               |  |
| subjects affected / exposed                     | 0 / 10 (0.00%) | 0 / 1 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         |  |
| Pain  |                |               |  |
| subjects affected / exposed                     | 0 / 10 (0.00%) | 0 / 1 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         |  |
| Pyrexia   |                |               |  |
| subjects affected / exposed                     | 0 / 10 (0.00%) | 0 / 1 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         |  |
| Immune system disorders                         |                |               |  |
| Hypersensitivity                                |                |               |  |
| subjects affected / exposed                     | 0 / 10 (0.00%) | 0 / 1 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         |  |
| Reproductive system and breast disorders        |                |               |  |
| Pelvic pain                                     |                |               |  |
| subjects affected / exposed                     | 0 / 10 (0.00%) | 0 / 1 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         |  |
| Respiratory, thoracic and mediastinal disorders |                |               |  |
| Acute respiratory failure                       |                |               |  |
| subjects affected / exposed                     | 0 / 10 (0.00%) | 0 / 1 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         |  |
| Dyspnoea  |                |               |  |

|   |                |                 |  |
|---|----------------|-----------------|--|
| subjects affected / exposed                     | 0 / 10 (0.00%) | 0 / 1 (0.00%)   |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           |  |
| Pneumonitis                                     |                |                 |  |
| subjects affected / exposed                     | 0 / 10 (0.00%) | 0 / 1 (0.00%)   |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           |  |
| Pneumothorax                                    |                |                 |  |
| subjects affected / exposed                     | 0 / 10 (0.00%) | 0 / 1 (0.00%)   |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           |  |
| Pulmonary embolism                              |                |                 |  |
| subjects affected / exposed                     | 0 / 10 (0.00%) | 0 / 1 (0.00%)   |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           |  |
| Respiratory failure                             |                |                 |  |
| subjects affected / exposed                     | 0 / 10 (0.00%) | 0 / 1 (0.00%)   |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           |  |
| Hypoxia   |                |                 |  |
| subjects affected / exposed                     | 0 / 10 (0.00%) | 1 / 1 (100.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           |  |
| Psychiatric disorders                           |                |                 |  |
| Confusional state                               |                |                 |  |
| subjects affected / exposed                     | 0 / 10 (0.00%) | 1 / 1 (100.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           |  |
| Mental status changes                           |                |                 |  |
| subjects affected / exposed                     | 0 / 10 (0.00%) | 1 / 1 (100.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           |  |
| Investigations                                  |                |                 |  |

|   |                |               |  |
|---|----------------|---------------|--|
| Alanine aminotransferase increased              |                |               |  |
| subjects affected / exposed                     | 0 / 10 (0.00%) | 0 / 1 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         |  |
| Aspartate aminotransferase increased            |                |               |  |
| subjects affected / exposed                     | 0 / 10 (0.00%) | 0 / 1 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         |  |
| Blood alkaline phosphatase increased            |                |               |  |
| subjects affected / exposed                     | 0 / 10 (0.00%) | 0 / 1 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         |  |
| Blood bilirubin increased                       |                |               |  |
| subjects affected / exposed                     | 0 / 10 (0.00%) | 0 / 1 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         |  |
| Hepatic enzyme increased                        |                |               |  |
| subjects affected / exposed                     | 0 / 10 (0.00%) | 0 / 1 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         |  |
| Lipase increased                                |                |               |  |
| subjects affected / exposed                     | 0 / 10 (0.00%) | 0 / 1 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         |  |
| Injury, poisoning and procedural complications  |                |               |  |
| Brain herniation                                |                |               |  |
| subjects affected / exposed                     | 0 / 10 (0.00%) | 0 / 1 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         |  |
| Lower limb fracture                             |                |               |  |
| subjects affected / exposed                     | 0 / 10 (0.00%) | 0 / 1 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         |  |

|   |                |                 |  |
|---|----------------|-----------------|--|
| Fall  |                |                 |  |
| subjects affected / exposed                     | 0 / 10 (0.00%) | 1 / 1 (100.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           |  |
| Cardiac disorders                               |                |                 |  |
| Acute myocardial infarction                     |                |                 |  |
| subjects affected / exposed                     | 0 / 10 (0.00%) | 0 / 1 (0.00%)   |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           |  |
| Atrial fibrillation                             |                |                 |  |
| subjects affected / exposed                     | 0 / 10 (0.00%) | 0 / 1 (0.00%)   |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           |  |
| Cardiac failure                                 |                |                 |  |
| subjects affected / exposed                     | 0 / 10 (0.00%) | 0 / 1 (0.00%)   |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           |  |
| Cardiac failure congestive                      |                |                 |  |
| subjects affected / exposed                     | 0 / 10 (0.00%) | 0 / 1 (0.00%)   |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           |  |
| Myocardial infarction                           |                |                 |  |
| subjects affected / exposed                     | 0 / 10 (0.00%) | 0 / 1 (0.00%)   |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           |  |
| Nervous system disorders                        |                |                 |  |
| Aphasia   |                |                 |  |
| subjects affected / exposed                     | 0 / 10 (0.00%) | 0 / 1 (0.00%)   |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           |  |
| Arachnoiditis                                   |                |                 |  |
| subjects affected / exposed                     | 0 / 10 (0.00%) | 0 / 1 (0.00%)   |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           |  |



|   |                 |               |  |
|---|-----------------|---------------|--|
| Dizziness                                       |                 |               |  |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Dysaesthesia                                    |                 |               |  |
| subjects affected / exposed                     | 1 / 10 (10.00%) | 0 / 1 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Guillain-Barre syndrome                         |                 |               |  |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Hemiparesis                                     |                 |               |  |
| subjects affected / exposed                     | 1 / 10 (10.00%) | 0 / 1 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Monoplegia                                      |                 |               |  |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Nervous system disorder                         |                 |               |  |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Nystagmus                                       |                 |               |  |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Paraesthesia                                    |                 |               |  |
| subjects affected / exposed                     | 1 / 10 (10.00%) | 0 / 1 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Seizure   |                 |               |  |

|   |                 |               |  |
|---|-----------------|---------------|--|
| subjects affected / exposed                     | 1 / 10 (10.00%) | 0 / 1 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| <b>Blood and lymphatic system disorders</b>     |                 |               |  |
| <b>Anaemia</b>                                  |                 |               |  |
| subjects affected / exposed                     | 1 / 10 (10.00%) | 0 / 1 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| <b>Autoimmune haemolytic anaemia</b>            |                 |               |  |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| <b>Immune thrombocytopenic purpura</b>          |                 |               |  |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| <b>Thrombocytopenia</b>                         |                 |               |  |
| subjects affected / exposed                     | 1 / 10 (10.00%) | 0 / 1 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| <b>Eye disorders</b>                            |                 |               |  |
| <b>Iridocyclitis</b>                            |                 |               |  |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| <b>Gastrointestinal disorders</b>               |                 |               |  |
| <b>Abdominal pain</b>                           |                 |               |  |
| subjects affected / exposed                     | 1 / 10 (10.00%) | 0 / 1 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| <b>Autoimmune colitis</b>                       |                 |               |  |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |

|   |                |               |  |
|---|----------------|---------------|--|
| Colitis   |                |               |  |
| subjects affected / exposed                     | 0 / 10 (0.00%) | 0 / 1 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         |  |
| Constipation                                    |                |               |  |
| subjects affected / exposed                     | 0 / 10 (0.00%) | 0 / 1 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         |  |
| Diarrhoea                                       |                |               |  |
| subjects affected / exposed                     | 0 / 10 (0.00%) | 0 / 1 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         |  |
| Enterocolitis                                   |                |               |  |
| subjects affected / exposed                     | 0 / 10 (0.00%) | 0 / 1 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         |  |
| Intestinal ischaemia                            |                |               |  |
| subjects affected / exposed                     | 0 / 10 (0.00%) | 0 / 1 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         |  |
| Intra-abdominal fluid collection                |                |               |  |
| subjects affected / exposed                     | 0 / 10 (0.00%) | 0 / 1 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         |  |
| Necrotising oesophagitis                        |                |               |  |
| subjects affected / exposed                     | 0 / 10 (0.00%) | 0 / 1 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         |  |
| Pancreatitis                                    |                |               |  |
| subjects affected / exposed                     | 0 / 10 (0.00%) | 0 / 1 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         |  |
| Small intestinal obstruction                    |                |               |  |

|   |                |                 |  |
|---|----------------|-----------------|--|
| subjects affected / exposed                     | 0 / 10 (0.00%) | 0 / 1 (0.00%)   |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           |  |
| Volvulus  |                |                 |  |
| subjects affected / exposed                     | 0 / 10 (0.00%) | 0 / 1 (0.00%)   |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           |  |
| Vomiting  |                |                 |  |
| subjects affected / exposed                     | 0 / 10 (0.00%) | 1 / 1 (100.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           |  |
| Nausea  |                |                 |  |
| subjects affected / exposed                     | 0 / 10 (0.00%) | 1 / 1 (100.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           |  |
| Hepatobiliary disorders                         |                |                 |  |
| Autoimmune hepatitis                            |                |                 |  |
| subjects affected / exposed                     | 0 / 10 (0.00%) | 0 / 1 (0.00%)   |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           |  |
| Bile duct obstruction                           |                |                 |  |
| subjects affected / exposed                     | 0 / 10 (0.00%) | 0 / 1 (0.00%)   |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           |  |
| Hepatitis                                       |                |                 |  |
| subjects affected / exposed                     | 0 / 10 (0.00%) | 0 / 1 (0.00%)   |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           |  |
| Hepatotoxicity                                  |                |                 |  |
| subjects affected / exposed                     | 0 / 10 (0.00%) | 0 / 1 (0.00%)   |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           |  |
| Immune-mediated hepatitis                       |                |                 |  |

|   |                |               |  |
|---|----------------|---------------|--|
| subjects affected / exposed                           | 0 / 10 (0.00%) | 0 / 1 (0.00%) |  |
| occurrences causally related to treatment / all       | 0 / 0          | 0 / 0         |  |
| deaths causally related to treatment / all            | 0 / 0          | 0 / 0         |  |
| Liver disorder  |                |               |  |
| subjects affected / exposed                           | 0 / 10 (0.00%) | 0 / 1 (0.00%) |  |
| occurrences causally related to treatment / all       | 0 / 0          | 0 / 0         |  |
| deaths causally related to treatment / all            | 0 / 0          | 0 / 0         |  |
| Skin and subcutaneous tissue disorders                |                |               |  |
| Drug reaction with eosinophilia and systemic symptoms |                |               |  |
| subjects affected / exposed                           | 0 / 10 (0.00%) | 0 / 1 (0.00%) |  |
| occurrences causally related to treatment / all       | 0 / 0          | 0 / 0         |  |
| deaths causally related to treatment / all            | 0 / 0          | 0 / 0         |  |
| Rash  |                |               |  |
| subjects affected / exposed                           | 0 / 10 (0.00%) | 0 / 1 (0.00%) |  |
| occurrences causally related to treatment / all       | 0 / 0          | 0 / 0         |  |
| deaths causally related to treatment / all            | 0 / 0          | 0 / 0         |  |
| Renal and urinary disorders                           |                |               |  |
| Acute kidney injury                                   |                |               |  |
| subjects affected / exposed                           | 0 / 10 (0.00%) | 0 / 1 (0.00%) |  |
| occurrences causally related to treatment / all       | 0 / 0          | 0 / 0         |  |
| deaths causally related to treatment / all            | 0 / 0          | 0 / 0         |  |
| Haematuria  |                |               |  |
| subjects affected / exposed                           | 0 / 10 (0.00%) | 0 / 1 (0.00%) |  |
| occurrences causally related to treatment / all       | 0 / 0          | 0 / 0         |  |
| deaths causally related to treatment / all            | 0 / 0          | 0 / 0         |  |
| Renal failure   |                |               |  |
| subjects affected / exposed                           | 0 / 10 (0.00%) | 0 / 1 (0.00%) |  |
| occurrences causally related to treatment / all       | 0 / 0          | 0 / 0         |  |
| deaths causally related to treatment / all            | 0 / 0          | 0 / 0         |  |
| Endocrine disorders                                   |                |               |  |
| Adrenal insufficiency                                 |                |               |  |
| subjects affected / exposed                           | 0 / 10 (0.00%) | 0 / 1 (0.00%) |  |
| occurrences causally related to treatment / all       | 0 / 0          | 0 / 0         |  |
| deaths causally related to treatment / all            | 0 / 0          | 0 / 0         |  |

|   |                 |               |  |
|---|-----------------|---------------|--|
| Hyperthyroidism                                 |                 |               |  |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Hypophysitis                                    |                 |               |  |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Musculoskeletal and connective tissue disorders |                 |               |  |
| Arthritis                                       |                 |               |  |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Back pain                                       |                 |               |  |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Bone disorder                                   |                 |               |  |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Flank pain                                      |                 |               |  |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Musculoskeletal chest pain                      |                 |               |  |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Pain in extremity                               |                 |               |  |
| subjects affected / exposed                     | 1 / 10 (10.00%) | 0 / 1 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |

|  |                                      |                                     |  |
|--|--------------------------------------|-------------------------------------|--|
| Infections and infestations<br>Clostridium difficile infection<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all | <br>0 / 10 (0.00%)<br>0 / 0<br>0 / 0 | <br>0 / 1 (0.00%)<br>0 / 0<br>0 / 0 |  |
| Encephalitis<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all   | <br>0 / 10 (0.00%)<br>0 / 0<br>0 / 0 | <br>0 / 1 (0.00%)<br>0 / 0<br>0 / 0 |  |
| Liver abscess<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all  | <br>0 / 10 (0.00%)<br>0 / 0<br>0 / 0 | <br>0 / 1 (0.00%)<br>0 / 0<br>0 / 0 |  |
| Meningitis<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all   | <br>0 / 10 (0.00%)<br>0 / 0<br>0 / 0 | <br>0 / 1 (0.00%)<br>0 / 0<br>0 / 0 |  |
| Pneumonia<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all  | <br>0 / 10 (0.00%)<br>0 / 0<br>0 / 0 | <br>0 / 1 (0.00%)<br>0 / 0<br>0 / 0 |  |
| Respiratory tract infection<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all                                    | <br>0 / 10 (0.00%)<br>0 / 0<br>0 / 0 | <br>0 / 1 (0.00%)<br>0 / 0<br>0 / 0 |  |
| Sepsis<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all   | <br>0 / 10 (0.00%)<br>0 / 0<br>0 / 0 | <br>0 / 1 (0.00%)<br>0 / 0<br>0 / 0 |  |
| Sinusitis<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all  | <br>0 / 10 (0.00%)<br>0 / 0<br>0 / 0 | <br>0 / 1 (0.00%)<br>0 / 0<br>0 / 0 |  |
| Staphylococcal infection   |                                      |                                     |  |

|   |                |                 |  |
|---|----------------|-----------------|--|
| subjects affected / exposed                     | 0 / 10 (0.00%) | 0 / 1 (0.00%)   |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           |  |
| Urinary tract infection                         |                |                 |  |
| subjects affected / exposed                     | 0 / 10 (0.00%) | 0 / 1 (0.00%)   |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           |  |
| Metabolism and nutrition disorders              |                |                 |  |
| Dehydration                                     |                |                 |  |
| subjects affected / exposed                     | 0 / 10 (0.00%) | 1 / 1 (100.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           |  |
| Failure to thrive                               |                |                 |  |
| subjects affected / exposed                     | 0 / 10 (0.00%) | 1 / 1 (100.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           |  |
| Hyperglycaemia                                  |                |                 |  |
| subjects affected / exposed                     | 0 / 10 (0.00%) | 0 / 1 (0.00%)   |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           |  |
| Hyperkalaemia                                   |                |                 |  |
| subjects affected / exposed                     | 0 / 10 (0.00%) | 0 / 1 (0.00%)   |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           |  |
| Hypokalaemia                                    |                |                 |  |
| subjects affected / exposed                     | 0 / 10 (0.00%) | 0 / 1 (0.00%)   |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           |  |
| Hyponatraemia                                   |                |                 |  |
| subjects affected / exposed                     | 0 / 10 (0.00%) | 0 / 1 (0.00%)   |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           |  |



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

| <b>Non-serious adverse events</b>                                   | <b>N3 60M NAIVE</b> | <b>N1 60M + I3 90M,<br/>W2</b> | <b>N1 60M + I3 90M,<br/>W4</b> |
|---|---------------------|--------------------------------|--------------------------------|
| Total subjects affected by non-serious adverse events               |                     |                                |                                |
| subjects affected / exposed   | 41 / 41 (100.00%)   | 11 / 11 (100.00%)              | 10 / 10 (100.00%)              |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                     |                                |                                |
| Malignant neoplasm progression                                      |                     |                                |                                |
| subjects affected / exposed   | 0 / 41 (0.00%)      | 0 / 11 (0.00%)                 | 1 / 10 (10.00%)                |
| occurrences (all)   | 0                   | 0                              | 1                              |
| Tumour pain   |                     |                                |                                |
| subjects affected / exposed   | 3 / 41 (7.32%)      | 1 / 11 (9.09%)                 | 2 / 10 (20.00%)                |
| occurrences (all)   | 3                   | 1                              | 2                              |
| Tumour embolism   |                     |                                |                                |
| subjects affected / exposed   | 0 / 41 (0.00%)      | 0 / 11 (0.00%)                 | 1 / 10 (10.00%)                |
| occurrences (all)   | 0                   | 0                              | 1                              |
| Oncologic complication  |                     |                                |                                |
| subjects affected / exposed   | 0 / 41 (0.00%)      | 0 / 11 (0.00%)                 | 0 / 10 (0.00%)                 |
| occurrences (all)   | 0                   | 0                              | 0                              |
| Vascular disorders  |                     |                                |                                |
| Embolism  |                     |                                |                                |
| subjects affected / exposed   | 2 / 41 (4.88%)      | 0 / 11 (0.00%)                 | 0 / 10 (0.00%)                 |
| occurrences (all)   | 2                   | 0                              | 0                              |
| Flushing  |                     |                                |                                |
| subjects affected / exposed   | 1 / 41 (2.44%)      | 0 / 11 (0.00%)                 | 0 / 10 (0.00%)                 |
| occurrences (all)   | 1                   | 0                              | 0                              |
| Hypertension  |                     |                                |                                |
| subjects affected / exposed   | 6 / 41 (14.63%)     | 0 / 11 (0.00%)                 | 1 / 10 (10.00%)                |
| occurrences (all)   | 8                   | 0                              | 1                              |
| Hypotension   |                     |                                |                                |
| subjects affected / exposed   | 0 / 41 (0.00%)      | 1 / 11 (9.09%)                 | 1 / 10 (10.00%)                |
| occurrences (all)   | 0                   | 1                              | 1                              |
| Lymphoedema   |                     |                                |                                |
| subjects affected / exposed   | 2 / 41 (4.88%)      | 1 / 11 (9.09%)                 | 1 / 10 (10.00%)                |
| occurrences (all)   | 2                   | 1                              | 1                              |
| Hot flush   |                     |                                |                                |

|  |                  |                 |                 |
|--|------------------|-----------------|-----------------|
| subjects affected / exposed                          | 1 / 41 (2.44%)   | 1 / 11 (9.09%)  | 0 / 10 (0.00%)  |
| occurrences (all)                                    | 1                | 1               | 0               |
| Orthostatic hypotension                              |                  |                 |                 |
| subjects affected / exposed                          | 0 / 41 (0.00%)   | 0 / 11 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)                                    | 0                | 0               | 0               |
| General disorders and administration site conditions |                  |                 |                 |
| Asthenia   |                  |                 |                 |
| subjects affected / exposed                          | 3 / 41 (7.32%)   | 3 / 11 (27.27%) | 2 / 10 (20.00%) |
| occurrences (all)                                    | 3                | 3               | 2               |
| Chest pain   |                  |                 |                 |
| subjects affected / exposed                          | 1 / 41 (2.44%)   | 0 / 11 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)                                    | 2                | 0               | 0               |
| Chills   |                  |                 |                 |
| subjects affected / exposed                          | 3 / 41 (7.32%)   | 3 / 11 (27.27%) | 4 / 10 (40.00%) |
| occurrences (all)                                    | 3                | 3               | 5               |
| Fatigue  |                  |                 |                 |
| subjects affected / exposed                          | 21 / 41 (51.22%) | 7 / 11 (63.64%) | 4 / 10 (40.00%) |
| occurrences (all)                                    | 32               | 7               | 5               |
| Hernia pain  |                  |                 |                 |
| subjects affected / exposed                          | 0 / 41 (0.00%)   | 0 / 11 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)                                    | 0                | 0               | 0               |
| Influenza like illness                               |                  |                 |                 |
| subjects affected / exposed                          | 4 / 41 (9.76%)   | 2 / 11 (18.18%) | 1 / 10 (10.00%) |
| occurrences (all)                                    | 6                | 3               | 1               |
| Localised oedema                                     |                  |                 |                 |
| subjects affected / exposed                          | 0 / 41 (0.00%)   | 0 / 11 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)                                    | 0                | 0               | 0               |
| Malaise  |                  |                 |                 |
| subjects affected / exposed                          | 0 / 41 (0.00%)   | 0 / 11 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)                                    | 0                | 0               | 0               |
| Mucosal inflammation                                 |                  |                 |                 |
| subjects affected / exposed                          | 3 / 41 (7.32%)   | 0 / 11 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)                                    | 3                | 0               | 0               |
| Non-cardiac chest pain                               |                  |                 |                 |

|                                    |                  |                 |                 |
|------------------------------------|------------------|-----------------|-----------------|
| subjects affected / exposed        | 2 / 41 (4.88%)   | 0 / 11 (0.00%)  | 1 / 10 (10.00%) |
| occurrences (all)                  | 3                | 0               | 1               |
| Oedema peripheral                  |                  |                 |                 |
| subjects affected / exposed        | 9 / 41 (21.95%)  | 1 / 11 (9.09%)  | 3 / 10 (30.00%) |
| occurrences (all)                  | 10               | 1               | 4               |
| Pain                               |                  |                 |                 |
| subjects affected / exposed        | 3 / 41 (7.32%)   | 0 / 11 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)                  | 5                | 0               | 0               |
| Peripheral swelling                |                  |                 |                 |
| subjects affected / exposed        | 1 / 41 (2.44%)   | 1 / 11 (9.09%)  | 1 / 10 (10.00%) |
| occurrences (all)                  | 1                | 1               | 1               |
| Pyrexia                            |                  |                 |                 |
| subjects affected / exposed        | 11 / 41 (26.83%) | 6 / 11 (54.55%) | 6 / 10 (60.00%) |
| occurrences (all)                  | 12               | 7               | 7               |
| Temperature intolerance            |                  |                 |                 |
| subjects affected / exposed        | 0 / 41 (0.00%)   | 0 / 11 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)                  | 0                | 0               | 0               |
| Decreased activity                 |                  |                 |                 |
| subjects affected / exposed        | 0 / 41 (0.00%)   | 1 / 11 (9.09%)  | 0 / 10 (0.00%)  |
| occurrences (all)                  | 0                | 1               | 0               |
| Feeling cold                       |                  |                 |                 |
| subjects affected / exposed        | 0 / 41 (0.00%)   | 1 / 11 (9.09%)  | 0 / 10 (0.00%)  |
| occurrences (all)                  | 0                | 1               | 0               |
| Gait disturbance                   |                  |                 |                 |
| subjects affected / exposed        | 0 / 41 (0.00%)   | 1 / 11 (9.09%)  | 0 / 10 (0.00%)  |
| occurrences (all)                  | 0                | 1               | 0               |
| Feeling of body temperature change |                  |                 |                 |
| subjects affected / exposed        | 0 / 41 (0.00%)   | 1 / 11 (9.09%)  | 0 / 10 (0.00%)  |
| occurrences (all)                  | 0                | 1               | 0               |
| Inflammation                       |                  |                 |                 |
| subjects affected / exposed        | 1 / 41 (2.44%)   | 1 / 11 (9.09%)  | 0 / 10 (0.00%)  |
| occurrences (all)                  | 1                | 1               | 0               |
| Physical deconditioning            |                  |                 |                 |
| subjects affected / exposed        | 0 / 41 (0.00%)   | 1 / 11 (9.09%)  | 0 / 10 (0.00%)  |
| occurrences (all)                  | 0                | 1               | 0               |
| Axillary pain                      |                  |                 |                 |

|  |                     |                     |                     |
|--|---------------------|---------------------|---------------------|
| subjects affected / exposed<br>occurrences (all) | 1 / 41 (2.44%)<br>1 | 0 / 11 (0.00%)<br>0 | 0 / 10 (0.00%)<br>0 |
| Immune system disorders                          |                     |                     |                     |
| Drug hypersensitivity                            |                     |                     |                     |
| subjects affected / exposed                      | 0 / 41 (0.00%)      | 0 / 11 (0.00%)      | 0 / 10 (0.00%)      |
| occurrences (all)                                | 0                   | 0                   | 0                   |
| Hypersensitivity                                 |                     |                     |                     |
| subjects affected / exposed                      | 1 / 41 (2.44%)      | 2 / 11 (18.18%)     | 0 / 10 (0.00%)      |
| occurrences (all)                                | 1                   | 2                   | 0                   |
| Reproductive system and breast disorders         |                     |                     |                     |
| Nipple pain                                      |                     |                     |                     |
| subjects affected / exposed                      | 0 / 41 (0.00%)      | 0 / 11 (0.00%)      | 0 / 10 (0.00%)      |
| occurrences (all)                                | 0                   | 0                   | 0                   |
| Spermatic cord haemorrhage                       |                     |                     |                     |
| subjects affected / exposed                      | 0 / 41 (0.00%)      | 0 / 11 (0.00%)      | 0 / 10 (0.00%)      |
| occurrences (all)                                | 0                   | 0                   | 0                   |
| Genital rash                                     |                     |                     |                     |
| subjects affected / exposed                      | 1 / 41 (2.44%)      | 0 / 11 (0.00%)      | 1 / 10 (10.00%)     |
| occurrences (all)                                | 1                   | 0                   | 1                   |
| Scrotal swelling                                 |                     |                     |                     |
| subjects affected / exposed                      | 0 / 41 (0.00%)      | 1 / 11 (9.09%)      | 0 / 10 (0.00%)      |
| occurrences (all)                                | 0                   | 1                   | 0                   |
| Respiratory, thoracic and mediastinal disorders  |                     |                     |                     |
| Bronchial obstruction                            |                     |                     |                     |
| subjects affected / exposed                      | 0 / 41 (0.00%)      | 0 / 11 (0.00%)      | 0 / 10 (0.00%)      |
| occurrences (all)                                | 0                   | 0                   | 0                   |
| Cough  |                     |                     |                     |
| subjects affected / exposed                      | 10 / 41 (24.39%)    | 4 / 11 (36.36%)     | 3 / 10 (30.00%)     |
| occurrences (all)                                | 12                  | 4                   | 3                   |
| Dyspnoea   |                     |                     |                     |
| subjects affected / exposed                      | 3 / 41 (7.32%)      | 3 / 11 (27.27%)     | 3 / 10 (30.00%)     |
| occurrences (all)                                | 3                   | 3                   | 3                   |
| Hypoxia  |                     |                     |                     |
| subjects affected / exposed                      | 0 / 41 (0.00%)      | 1 / 11 (9.09%)      | 1 / 10 (10.00%)     |
| occurrences (all)                                | 0                   | 1                   | 1                   |
| Oropharyngeal pain                               |                     |                     |                     |

|                             |                 |                |                 |
|-----------------------------|-----------------|----------------|-----------------|
| subjects affected / exposed | 4 / 41 (9.76%)  | 0 / 11 (0.00%) | 0 / 10 (0.00%)  |
| occurrences (all)           | 4               | 0              | 0               |
| Nasal congestion            |                 |                |                 |
| subjects affected / exposed | 6 / 41 (14.63%) | 0 / 11 (0.00%) | 1 / 10 (10.00%) |
| occurrences (all)           | 7               | 0              | 1               |
| Pleural effusion            |                 |                |                 |
| subjects affected / exposed | 1 / 41 (2.44%)  | 0 / 11 (0.00%) | 3 / 10 (30.00%) |
| occurrences (all)           | 1               | 0              | 3               |
| Pneumonitis                 |                 |                |                 |
| subjects affected / exposed | 1 / 41 (2.44%)  | 1 / 11 (9.09%) | 1 / 10 (10.00%) |
| occurrences (all)           | 1               | 1              | 1               |
| Productive cough            |                 |                |                 |
| subjects affected / exposed | 2 / 41 (4.88%)  | 0 / 11 (0.00%) | 0 / 10 (0.00%)  |
| occurrences (all)           | 2               | 0              | 0               |
| Rhinitis allergic           |                 |                |                 |
| subjects affected / exposed | 0 / 41 (0.00%)  | 0 / 11 (0.00%) | 0 / 10 (0.00%)  |
| occurrences (all)           | 0               | 0              | 0               |
| Rhinorrhoea                 |                 |                |                 |
| subjects affected / exposed | 0 / 41 (0.00%)  | 0 / 11 (0.00%) | 2 / 10 (20.00%) |
| occurrences (all)           | 0               | 0              | 2               |
| Upper-airway cough syndrome |                 |                |                 |
| subjects affected / exposed | 0 / 41 (0.00%)  | 0 / 11 (0.00%) | 1 / 10 (10.00%) |
| occurrences (all)           | 0               | 0              | 1               |
| Dysphonia                   |                 |                |                 |
| subjects affected / exposed | 1 / 41 (2.44%)  | 1 / 11 (9.09%) | 0 / 10 (0.00%)  |
| occurrences (all)           | 1               | 1              | 0               |
| Dyspnoea exertional         |                 |                |                 |
| subjects affected / exposed | 1 / 41 (2.44%)  | 1 / 11 (9.09%) | 0 / 10 (0.00%)  |
| occurrences (all)           | 1               | 1              | 0               |
| Epistaxis                   |                 |                |                 |
| subjects affected / exposed | 0 / 41 (0.00%)  | 1 / 11 (9.09%) | 0 / 10 (0.00%)  |
| occurrences (all)           | 0               | 1              | 0               |
| Haemoptysis                 |                 |                |                 |
| subjects affected / exposed | 0 / 41 (0.00%)  | 0 / 11 (0.00%) | 1 / 10 (10.00%) |
| occurrences (all)           | 0               | 0              | 1               |
| Hiccups                     |                 |                |                 |

|  |                      |                     |                      |
|--|----------------------|---------------------|----------------------|
| subjects affected / exposed<br>occurrences (all)                                 | 0 / 41 (0.00%)<br>0  | 0 / 11 (0.00%)<br>0 | 0 / 10 (0.00%)<br>0  |
| Pulmonary embolism<br>subjects affected / exposed<br>occurrences (all)           | 2 / 41 (4.88%)<br>2  | 1 / 11 (9.09%)<br>1 | 0 / 10 (0.00%)<br>0  |
| Respiratory failure<br>subjects affected / exposed<br>occurrences (all)          | 0 / 41 (0.00%)<br>0  | 0 / 11 (0.00%)<br>0 | 0 / 10 (0.00%)<br>0  |
| Respiratory tract congestion<br>subjects affected / exposed<br>occurrences (all) | 1 / 41 (2.44%)<br>3  | 0 / 11 (0.00%)<br>0 | 1 / 10 (10.00%)<br>1 |
| Psychiatric disorders  |                      |                     |                      |
| Confusional state<br>subjects affected / exposed<br>occurrences (all)            | 0 / 41 (0.00%)<br>0  | 1 / 11 (9.09%)<br>1 | 1 / 10 (10.00%)<br>1 |
| Anxiety<br>subjects affected / exposed<br>occurrences (all)                      | 2 / 41 (4.88%)<br>2  | 0 / 11 (0.00%)<br>0 | 2 / 10 (20.00%)<br>2 |
| Depression<br>subjects affected / exposed<br>occurrences (all)                   | 2 / 41 (4.88%)<br>2  | 1 / 11 (9.09%)<br>1 | 0 / 10 (0.00%)<br>0  |
| Insomnia<br>subjects affected / exposed<br>occurrences (all)                     | 6 / 41 (14.63%)<br>6 | 1 / 11 (9.09%)<br>1 | 3 / 10 (30.00%)<br>3 |
| Sleep disorder<br>subjects affected / exposed<br>occurrences (all)               | 0 / 41 (0.00%)<br>0  | 0 / 11 (0.00%)<br>0 | 0 / 10 (0.00%)<br>0  |
| Depressed mood<br>subjects affected / exposed<br>occurrences (all)               | 0 / 41 (0.00%)<br>0  | 0 / 11 (0.00%)<br>0 | 1 / 10 (10.00%)<br>1 |
| Disorientation<br>subjects affected / exposed<br>occurrences (all)               | 0 / 41 (0.00%)<br>0  | 1 / 11 (9.09%)<br>1 | 0 / 10 (0.00%)<br>0  |
| Irritability<br>subjects affected / exposed<br>occurrences (all)                 | 0 / 41 (0.00%)<br>0  | 0 / 11 (0.00%)<br>0 | 1 / 10 (10.00%)<br>1 |

|  |                 |                 |                 |
|--|-----------------|-----------------|-----------------|
| Hallucination<br>subjects affected / exposed                                   | 0 / 41 (0.00%)  | 1 / 11 (9.09%)  | 0 / 10 (0.00%)  |
| occurrences (all)  | 0               | 1               | 0               |
| Mental status changes<br>subjects affected / exposed                           | 0 / 41 (0.00%)  | 0 / 11 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)  | 0               | 0               | 0               |
| Investigations   |                 |                 |                 |
| Activated partial thromboplastin time prolonged<br>subjects affected / exposed | 0 / 41 (0.00%)  | 0 / 11 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)  | 0               | 0               | 0               |
| Alanine aminotransferase increased<br>subjects affected / exposed              | 6 / 41 (14.63%) | 5 / 11 (45.45%) | 3 / 10 (30.00%) |
| occurrences (all)  | 8               | 7               | 3               |
| Amylase increased<br>subjects affected / exposed                               | 2 / 41 (4.88%)  | 0 / 11 (0.00%)  | 1 / 10 (10.00%) |
| occurrences (all)  | 2               | 0               | 1               |
| Aspartate aminotransferase increased<br>subjects affected / exposed            | 6 / 41 (14.63%) | 6 / 11 (54.55%) | 3 / 10 (30.00%) |
| occurrences (all)  | 11              | 9               | 3               |
| Blood alkaline phosphatase increased<br>subjects affected / exposed            | 5 / 41 (12.20%) | 0 / 11 (0.00%)  | 1 / 10 (10.00%) |
| occurrences (all)  | 10              | 0               | 1               |
| Blood bilirubin increased<br>subjects affected / exposed                       | 2 / 41 (4.88%)  | 1 / 11 (9.09%)  | 2 / 10 (20.00%) |
| occurrences (all)  | 4               | 3               | 2               |
| Blood creatinine increased<br>subjects affected / exposed                      | 1 / 41 (2.44%)  | 1 / 11 (9.09%)  | 1 / 10 (10.00%) |
| occurrences (all)  | 2               | 1               | 1               |
| Blood thyroid stimulating hormone decreased<br>subjects affected / exposed     | 1 / 41 (2.44%)  | 0 / 11 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)  | 1               | 0               | 0               |
| Blood thyroid stimulating hormone increased<br>subjects affected / exposed     | 1 / 41 (2.44%)  | 0 / 11 (0.00%)  | 1 / 10 (10.00%) |
| occurrences (all)  | 1               | 0               | 1               |

|  |                 |                 |                 |
|--|-----------------|-----------------|-----------------|
| Cortisol increased                       |                 |                 |                 |
| subjects affected / exposed              | 0 / 41 (0.00%)  | 0 / 11 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)                        | 0               | 0               | 0               |
| Hepatic enzyme increased                 |                 |                 |                 |
| subjects affected / exposed              | 0 / 41 (0.00%)  | 0 / 11 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)                        | 0               | 0               | 0               |
| International normalised ratio increased |                 |                 |                 |
| subjects affected / exposed              | 0 / 41 (0.00%)  | 0 / 11 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)                        | 0               | 0               | 0               |
| Lipase increased                         |                 |                 |                 |
| subjects affected / exposed              | 8 / 41 (19.51%) | 2 / 11 (18.18%) | 2 / 10 (20.00%) |
| occurrences (all)                        | 15              | 3               | 4               |
| Lymphocyte count decreased               |                 |                 |                 |
| subjects affected / exposed              | 4 / 41 (9.76%)  | 1 / 11 (9.09%)  | 0 / 10 (0.00%)  |
| occurrences (all)                        | 8               | 1               | 0               |
| Platelet count decreased                 |                 |                 |                 |
| subjects affected / exposed              | 1 / 41 (2.44%)  | 2 / 11 (18.18%) | 0 / 10 (0.00%)  |
| occurrences (all)                        | 1               | 3               | 0               |
| Norovirus test positive                  |                 |                 |                 |
| subjects affected / exposed              | 0 / 41 (0.00%)  | 0 / 11 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)                        | 0               | 0               | 0               |
| Transaminases increased                  |                 |                 |                 |
| subjects affected / exposed              | 0 / 41 (0.00%)  | 0 / 11 (0.00%)  | 1 / 10 (10.00%) |
| occurrences (all)                        | 0               | 0               | 1               |
| Weight decreased                         |                 |                 |                 |
| subjects affected / exposed              | 8 / 41 (19.51%) | 2 / 11 (18.18%) | 2 / 10 (20.00%) |
| occurrences (all)                        | 8               | 2               | 2               |
| Weight increased                         |                 |                 |                 |
| subjects affected / exposed              | 1 / 41 (2.44%)  | 0 / 11 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)                        | 1               | 0               | 0               |
| Blood urea increased                     |                 |                 |                 |
| subjects affected / exposed              | 0 / 41 (0.00%)  | 0 / 11 (0.00%)  | 1 / 10 (10.00%) |
| occurrences (all)                        | 0               | 0               | 1               |
| Heart rate increased                     |                 |                 |                 |



|  |                     |                     |                     |
|--|---------------------|---------------------|---------------------|
| subjects affected / exposed<br>occurrences (all) | 0 / 41 (0.00%)<br>0 | 1 / 11 (9.09%)<br>1 | 0 / 10 (0.00%)<br>0 |
| Injury, poisoning and procedural complications   |                     |                     |                     |
| Contusion  |                     |                     |                     |
| subjects affected / exposed                      | 5 / 41 (12.20%)     | 0 / 11 (0.00%)      | 0 / 10 (0.00%)      |
| occurrences (all)                                | 5                   | 0                   | 0                   |
| Infusion related reaction                        |                     |                     |                     |
| subjects affected / exposed                      | 2 / 41 (4.88%)      | 0 / 11 (0.00%)      | 1 / 10 (10.00%)     |
| occurrences (all)                                | 2                   | 0                   | 1                   |
| Limb injury                                      |                     |                     |                     |
| subjects affected / exposed                      | 0 / 41 (0.00%)      | 0 / 11 (0.00%)      | 0 / 10 (0.00%)      |
| occurrences (all)                                | 0                   | 0                   | 0                   |
| Procedural pain                                  |                     |                     |                     |
| subjects affected / exposed                      | 0 / 41 (0.00%)      | 1 / 11 (9.09%)      | 0 / 10 (0.00%)      |
| occurrences (all)                                | 0                   | 1                   | 0                   |
| Bone fissure                                     |                     |                     |                     |
| subjects affected / exposed                      | 0 / 41 (0.00%)      | 0 / 11 (0.00%)      | 1 / 10 (10.00%)     |
| occurrences (all)                                | 0                   | 0                   | 1                   |
| Radiation pneumonitis                            |                     |                     |                     |
| subjects affected / exposed                      | 0 / 41 (0.00%)      | 0 / 11 (0.00%)      | 1 / 10 (10.00%)     |
| occurrences (all)                                | 0                   | 0                   | 1                   |
| Fall   |                     |                     |                     |
| subjects affected / exposed                      | 2 / 41 (4.88%)      | 0 / 11 (0.00%)      | 0 / 10 (0.00%)      |
| occurrences (all)                                | 2                   | 0                   | 0                   |
| Cardiac disorders                                |                     |                     |                     |
| Acute coronary syndrome                          |                     |                     |                     |
| subjects affected / exposed                      | 0 / 41 (0.00%)      | 0 / 11 (0.00%)      | 0 / 10 (0.00%)      |
| occurrences (all)                                | 0                   | 0                   | 0                   |
| Angina pectoris                                  |                     |                     |                     |
| subjects affected / exposed                      | 0 / 41 (0.00%)      | 0 / 11 (0.00%)      | 0 / 10 (0.00%)      |
| occurrences (all)                                | 0                   | 0                   | 0                   |
| Palpitations                                     |                     |                     |                     |
| subjects affected / exposed                      | 1 / 41 (2.44%)      | 0 / 11 (0.00%)      | 1 / 10 (10.00%)     |
| occurrences (all)                                | 1                   | 0                   | 1                   |
| Tachycardia                                      |                     |                     |                     |

|                                      |                  |                 |                 |
|--------------------------------------|------------------|-----------------|-----------------|
| subjects affected / exposed          | 0 / 41 (0.00%)   | 0 / 11 (0.00%)  | 2 / 10 (20.00%) |
| occurrences (all)                    | 0                | 0               | 2               |
| Cardiac failure congestive           |                  |                 |                 |
| subjects affected / exposed          | 0 / 41 (0.00%)   | 0 / 11 (0.00%)  | 1 / 10 (10.00%) |
| occurrences (all)                    | 0                | 0               | 1               |
| Atrioventricular block second degree |                  |                 |                 |
| subjects affected / exposed          | 0 / 41 (0.00%)   | 0 / 11 (0.00%)  | 1 / 10 (10.00%) |
| occurrences (all)                    | 0                | 0               | 1               |
| Nervous system disorders             |                  |                 |                 |
| Autonomic nervous system imbalance   |                  |                 |                 |
| subjects affected / exposed          | 0 / 41 (0.00%)   | 0 / 11 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)                    | 0                | 0               | 0               |
| Cerebrovascular accident             |                  |                 |                 |
| subjects affected / exposed          | 0 / 41 (0.00%)   | 0 / 11 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)                    | 0                | 0               | 0               |
| Disturbance in attention             |                  |                 |                 |
| subjects affected / exposed          | 0 / 41 (0.00%)   | 0 / 11 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)                    | 0                | 0               | 0               |
| Dizziness                            |                  |                 |                 |
| subjects affected / exposed          | 5 / 41 (12.20%)  | 1 / 11 (9.09%)  | 1 / 10 (10.00%) |
| occurrences (all)                    | 5                | 1               | 1               |
| Dysaesthesia                         |                  |                 |                 |
| subjects affected / exposed          | 0 / 41 (0.00%)   | 0 / 11 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)                    | 0                | 0               | 0               |
| Dysarthria                           |                  |                 |                 |
| subjects affected / exposed          | 1 / 41 (2.44%)   | 1 / 11 (9.09%)  | 0 / 10 (0.00%)  |
| occurrences (all)                    | 1                | 1               | 0               |
| Dysgeusia                            |                  |                 |                 |
| subjects affected / exposed          | 0 / 41 (0.00%)   | 2 / 11 (18.18%) | 2 / 10 (20.00%) |
| occurrences (all)                    | 0                | 2               | 2               |
| Headache                             |                  |                 |                 |
| subjects affected / exposed          | 10 / 41 (24.39%) | 0 / 11 (0.00%)  | 3 / 10 (30.00%) |
| occurrences (all)                    | 13               | 0               | 3               |
| Hemiparesis                          |                  |                 |                 |

|                             |                |                |                 |
|-----------------------------|----------------|----------------|-----------------|
| subjects affected / exposed | 0 / 41 (0.00%) | 0 / 11 (0.00%) | 0 / 10 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0               |
| Lethargy                    |                |                |                 |
| subjects affected / exposed | 0 / 41 (0.00%) | 0 / 11 (0.00%) | 1 / 10 (10.00%) |
| occurrences (all)           | 0              | 0              | 1               |
| Neuropathy peripheral       |                |                |                 |
| subjects affected / exposed | 0 / 41 (0.00%) | 1 / 11 (9.09%) | 1 / 10 (10.00%) |
| occurrences (all)           | 0              | 1              | 1               |
| Paraesthesia                |                |                |                 |
| subjects affected / exposed | 2 / 41 (4.88%) | 1 / 11 (9.09%) | 1 / 10 (10.00%) |
| occurrences (all)           | 2              | 1              | 2               |
| Presyncope                  |                |                |                 |
| subjects affected / exposed | 0 / 41 (0.00%) | 0 / 11 (0.00%) | 0 / 10 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0               |
| Restless legs syndrome      |                |                |                 |
| subjects affected / exposed | 0 / 41 (0.00%) | 0 / 11 (0.00%) | 0 / 10 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0               |
| Seizure                     |                |                |                 |
| subjects affected / exposed | 0 / 41 (0.00%) | 0 / 11 (0.00%) | 0 / 10 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0               |
| Aphasia                     |                |                |                 |
| subjects affected / exposed | 1 / 41 (2.44%) | 0 / 11 (0.00%) | 1 / 10 (10.00%) |
| occurrences (all)           | 1              | 0              | 1               |
| Amnesia                     |                |                |                 |
| subjects affected / exposed | 0 / 41 (0.00%) | 1 / 11 (9.09%) | 0 / 10 (0.00%)  |
| occurrences (all)           | 0              | 1              | 0               |
| Fine motor delay            |                |                |                 |
| subjects affected / exposed | 0 / 41 (0.00%) | 0 / 11 (0.00%) | 1 / 10 (10.00%) |
| occurrences (all)           | 0              | 0              | 1               |
| Encephalopathy              |                |                |                 |
| subjects affected / exposed | 0 / 41 (0.00%) | 0 / 11 (0.00%) | 1 / 10 (10.00%) |
| occurrences (all)           | 0              | 0              | 1               |
| Hypersomnia                 |                |                |                 |
| subjects affected / exposed | 0 / 41 (0.00%) | 1 / 11 (9.09%) | 0 / 10 (0.00%)  |
| occurrences (all)           | 0              | 1              | 0               |
| Hypoaesthesia               |                |                |                 |

|                                      |                 |                |                 |
|--------------------------------------|-----------------|----------------|-----------------|
| subjects affected / exposed          | 0 / 41 (0.00%)  | 1 / 11 (9.09%) | 0 / 10 (0.00%)  |
| occurrences (all)                    | 0               | 1              | 0               |
| Mental impairment                    |                 |                |                 |
| subjects affected / exposed          | 0 / 41 (0.00%)  | 1 / 11 (9.09%) | 0 / 10 (0.00%)  |
| occurrences (all)                    | 0               | 1              | 0               |
| Muscle spasticity                    |                 |                |                 |
| subjects affected / exposed          | 0 / 41 (0.00%)  | 0 / 11 (0.00%) | 1 / 10 (10.00%) |
| occurrences (all)                    | 0               | 0              | 1               |
| Neurotoxicity                        |                 |                |                 |
| subjects affected / exposed          | 0 / 41 (0.00%)  | 1 / 11 (9.09%) | 0 / 10 (0.00%)  |
| occurrences (all)                    | 0               | 1              | 0               |
| Somnolence                           |                 |                |                 |
| subjects affected / exposed          | 1 / 41 (2.44%)  | 1 / 11 (9.09%) | 0 / 10 (0.00%)  |
| occurrences (all)                    | 1               | 1              | 0               |
| Syncope                              |                 |                |                 |
| subjects affected / exposed          | 0 / 41 (0.00%)  | 0 / 11 (0.00%) | 1 / 10 (10.00%) |
| occurrences (all)                    | 0               | 0              | 1               |
| Spinal cord compression              |                 |                |                 |
| subjects affected / exposed          | 0 / 41 (0.00%)  | 1 / 11 (9.09%) | 0 / 10 (0.00%)  |
| occurrences (all)                    | 0               | 1              | 0               |
| Tremor                               |                 |                |                 |
| subjects affected / exposed          | 0 / 41 (0.00%)  | 0 / 11 (0.00%) | 1 / 10 (10.00%) |
| occurrences (all)                    | 0               | 0              | 1               |
| Balance disorder                     |                 |                |                 |
| subjects affected / exposed          | 0 / 41 (0.00%)  | 0 / 11 (0.00%) | 0 / 10 (0.00%)  |
| occurrences (all)                    | 0               | 0              | 0               |
| Blood and lymphatic system disorders |                 |                |                 |
| Anaemia                              |                 |                |                 |
| subjects affected / exposed          | 9 / 41 (21.95%) | 0 / 11 (0.00%) | 2 / 10 (20.00%) |
| occurrences (all)                    | 10              | 0              | 3               |
| Haemolytic anaemia                   |                 |                |                 |
| subjects affected / exposed          | 0 / 41 (0.00%)  | 0 / 11 (0.00%) | 0 / 10 (0.00%)  |
| occurrences (all)                    | 0               | 0              | 0               |
| Thrombocytopenia                     |                 |                |                 |
| subjects affected / exposed          | 2 / 41 (4.88%)  | 0 / 11 (0.00%) | 2 / 10 (20.00%) |
| occurrences (all)                    | 2               | 0              | 4               |

|   |                     |                     |                      |
|---|---------------------|---------------------|----------------------|
| Coagulopathy<br>subjects affected / exposed<br>occurrences (all)                              | 0 / 41 (0.00%)<br>0 | 0 / 11 (0.00%)<br>0 | 1 / 10 (10.00%)<br>1 |
| Lymphadenopathy<br>subjects affected / exposed<br>occurrences (all)                           | 0 / 41 (0.00%)<br>0 | 1 / 11 (9.09%)<br>1 | 0 / 10 (0.00%)<br>0  |
| Microcytic anaemia<br>subjects affected / exposed<br>occurrences (all)                        | 0 / 41 (0.00%)<br>0 | 0 / 11 (0.00%)<br>0 | 1 / 10 (10.00%)<br>1 |
| Ear and labyrinth disorders<br>Hypoacusis<br>subjects affected / exposed<br>occurrences (all) | 0 / 41 (0.00%)<br>0 | 0 / 11 (0.00%)<br>0 | 0 / 10 (0.00%)<br>0  |
| Cerumen impaction<br>subjects affected / exposed<br>occurrences (all)                         | 0 / 41 (0.00%)<br>0 | 0 / 11 (0.00%)<br>0 | 1 / 10 (10.00%)<br>1 |
| Eye disorders<br>Dry eye<br>subjects affected / exposed<br>occurrences (all)                  | 2 / 41 (4.88%)<br>2 | 1 / 11 (9.09%)<br>1 | 0 / 10 (0.00%)<br>0  |
| Eye disorder<br>subjects affected / exposed<br>occurrences (all)                              | 0 / 41 (0.00%)<br>0 | 0 / 11 (0.00%)<br>0 | 0 / 10 (0.00%)<br>0  |
| Eye pain<br>subjects affected / exposed<br>occurrences (all)                                  | 0 / 41 (0.00%)<br>0 | 0 / 11 (0.00%)<br>0 | 0 / 10 (0.00%)<br>0  |
| Uveitis<br>subjects affected / exposed<br>occurrences (all)                                   | 0 / 41 (0.00%)<br>0 | 1 / 11 (9.09%)<br>1 | 0 / 10 (0.00%)<br>0  |
| Vision blurred<br>subjects affected / exposed<br>occurrences (all)                            | 2 / 41 (4.88%)<br>3 | 0 / 11 (0.00%)<br>0 | 0 / 10 (0.00%)<br>0  |
| Visual impairment<br>subjects affected / exposed<br>occurrences (all)                         | 0 / 41 (0.00%)<br>0 | 0 / 11 (0.00%)<br>0 | 0 / 10 (0.00%)<br>0  |
| Eye pruritus  |                     |                     |                      |

|                             |                  |                 |                 |
|-----------------------------|------------------|-----------------|-----------------|
| subjects affected / exposed | 1 / 41 (2.44%)   | 1 / 11 (9.09%)  | 0 / 10 (0.00%)  |
| occurrences (all)           | 1                | 1               | 0               |
| Eye swelling                |                  |                 |                 |
| subjects affected / exposed | 0 / 41 (0.00%)   | 1 / 11 (9.09%)  | 0 / 10 (0.00%)  |
| occurrences (all)           | 0                | 1               | 0               |
| Iridocyclitis               |                  |                 |                 |
| subjects affected / exposed | 0 / 41 (0.00%)   | 0 / 11 (0.00%)  | 1 / 10 (10.00%) |
| occurrences (all)           | 0                | 0               | 1               |
| Lacrimation increased       |                  |                 |                 |
| subjects affected / exposed | 1 / 41 (2.44%)   | 1 / 11 (9.09%)  | 0 / 10 (0.00%)  |
| occurrences (all)           | 1                | 1               | 0               |
| Ocular hyperaemia           |                  |                 |                 |
| subjects affected / exposed | 0 / 41 (0.00%)   | 0 / 11 (0.00%)  | 1 / 10 (10.00%) |
| occurrences (all)           | 0                | 0               | 1               |
| Conjunctival oedema         |                  |                 |                 |
| subjects affected / exposed | 0 / 41 (0.00%)   | 0 / 11 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)           | 0                | 0               | 0               |
| Gastrointestinal disorders  |                  |                 |                 |
| Abdominal discomfort        |                  |                 |                 |
| subjects affected / exposed | 0 / 41 (0.00%)   | 0 / 11 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)           | 0                | 0               | 0               |
| Abdominal distension        |                  |                 |                 |
| subjects affected / exposed | 2 / 41 (4.88%)   | 1 / 11 (9.09%)  | 1 / 10 (10.00%) |
| occurrences (all)           | 2                | 1               | 1               |
| Abdominal pain              |                  |                 |                 |
| subjects affected / exposed | 11 / 41 (26.83%) | 3 / 11 (27.27%) | 1 / 10 (10.00%) |
| occurrences (all)           | 14               | 3               | 1               |
| Abdominal pain upper        |                  |                 |                 |
| subjects affected / exposed | 2 / 41 (4.88%)   | 1 / 11 (9.09%)  | 0 / 10 (0.00%)  |
| occurrences (all)           | 2                | 1               | 0               |
| Anal pruritus               |                  |                 |                 |
| subjects affected / exposed | 0 / 41 (0.00%)   | 0 / 11 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)           | 0                | 0               | 0               |
| Colitis                     |                  |                 |                 |
| subjects affected / exposed | 0 / 41 (0.00%)   | 0 / 11 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)           | 0                | 0               | 0               |

|                              |                  |                 |                 |
|------------------------------|------------------|-----------------|-----------------|
| Constipation                 |                  |                 |                 |
| subjects affected / exposed  | 11 / 41 (26.83%) | 4 / 11 (36.36%) | 2 / 10 (20.00%) |
| occurrences (all)            | 13               | 4               | 3               |
| Diarrhoea                    |                  |                 |                 |
| subjects affected / exposed  | 15 / 41 (36.59%) | 5 / 11 (45.45%) | 5 / 10 (50.00%) |
| occurrences (all)            | 23               | 5               | 6               |
| Dry mouth                    |                  |                 |                 |
| subjects affected / exposed  | 3 / 41 (7.32%)   | 0 / 11 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)            | 3                | 0               | 0               |
| Dyspepsia                    |                  |                 |                 |
| subjects affected / exposed  | 2 / 41 (4.88%)   | 0 / 11 (0.00%)  | 1 / 10 (10.00%) |
| occurrences (all)            | 2                | 0               | 1               |
| Dysphagia                    |                  |                 |                 |
| subjects affected / exposed  | 0 / 41 (0.00%)   | 0 / 11 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)            | 0                | 0               | 0               |
| Gastritis                    |                  |                 |                 |
| subjects affected / exposed  | 0 / 41 (0.00%)   | 1 / 11 (9.09%)  | 0 / 10 (0.00%)  |
| occurrences (all)            | 0                | 1               | 0               |
| Flatulence                   |                  |                 |                 |
| subjects affected / exposed  | 0 / 41 (0.00%)   | 0 / 11 (0.00%)  | 1 / 10 (10.00%) |
| occurrences (all)            | 0                | 0               | 1               |
| Gastrointestinal haemorrhage |                  |                 |                 |
| subjects affected / exposed  | 0 / 41 (0.00%)   | 0 / 11 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)            | 0                | 0               | 0               |
| Haemorrhoids                 |                  |                 |                 |
| subjects affected / exposed  | 1 / 41 (2.44%)   | 1 / 11 (9.09%)  | 0 / 10 (0.00%)  |
| occurrences (all)            | 1                | 1               | 0               |
| Nausea                       |                  |                 |                 |
| subjects affected / exposed  | 9 / 41 (21.95%)  | 3 / 11 (27.27%) | 2 / 10 (20.00%) |
| occurrences (all)            | 16               | 4               | 2               |
| Oral pain                    |                  |                 |                 |
| subjects affected / exposed  | 0 / 41 (0.00%)   | 0 / 11 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)            | 0                | 0               | 0               |
| Stomatitis                   |                  |                 |                 |
| subjects affected / exposed  | 4 / 41 (9.76%)   | 0 / 11 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)            | 4                | 0               | 0               |

|                                  |                 |                 |                 |
|----------------------------------|-----------------|-----------------|-----------------|
| Vomiting                         |                 |                 |                 |
| subjects affected / exposed      | 6 / 41 (14.63%) | 2 / 11 (18.18%) | 2 / 10 (20.00%) |
| occurrences (all)                | 10              | 3               | 2               |
| Abdominal tenderness             |                 |                 |                 |
| subjects affected / exposed      | 0 / 41 (0.00%)  | 0 / 11 (0.00%)  | 1 / 10 (10.00%) |
| occurrences (all)                | 0               | 0               | 1               |
| Aphthous ulcer                   |                 |                 |                 |
| subjects affected / exposed      | 0 / 41 (0.00%)  | 1 / 11 (9.09%)  | 0 / 10 (0.00%)  |
| occurrences (all)                | 0               | 1               | 0               |
| Autoimmune colitis               |                 |                 |                 |
| subjects affected / exposed      | 0 / 41 (0.00%)  | 1 / 11 (9.09%)  | 0 / 10 (0.00%)  |
| occurrences (all)                | 0               | 1               | 0               |
| Ascites                          |                 |                 |                 |
| subjects affected / exposed      | 1 / 41 (2.44%)  | 0 / 11 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)                | 1               | 0               | 0               |
| Chronic gastritis                |                 |                 |                 |
| subjects affected / exposed      | 0 / 41 (0.00%)  | 0 / 11 (0.00%)  | 1 / 10 (10.00%) |
| occurrences (all)                | 0               | 0               | 1               |
| Faecaloma                        |                 |                 |                 |
| subjects affected / exposed      | 0 / 41 (0.00%)  | 1 / 11 (9.09%)  | 0 / 10 (0.00%)  |
| occurrences (all)                | 0               | 1               | 0               |
| Gastrooesophageal reflux disease |                 |                 |                 |
| subjects affected / exposed      | 2 / 41 (4.88%)  | 1 / 11 (9.09%)  | 0 / 10 (0.00%)  |
| occurrences (all)                | 2               | 1               | 0               |
| Hepatobiliary disorders          |                 |                 |                 |
| Hepatic pain                     |                 |                 |                 |
| subjects affected / exposed      | 0 / 41 (0.00%)  | 0 / 11 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)                | 0               | 0               | 0               |
| Hypertransaminaemia              |                 |                 |                 |
| subjects affected / exposed      | 0 / 41 (0.00%)  | 1 / 11 (9.09%)  | 1 / 10 (10.00%) |
| occurrences (all)                | 0               | 1               | 1               |
| Bile duct obstruction            |                 |                 |                 |
| subjects affected / exposed      | 0 / 41 (0.00%)  | 0 / 11 (0.00%)  | 1 / 10 (10.00%) |
| occurrences (all)                | 0               | 0               | 1               |
| Cholelithiasis                   |                 |                 |                 |



|  |                     |                     |                      |
|--|---------------------|---------------------|----------------------|
| subjects affected / exposed<br>occurrences (all) | 0 / 41 (0.00%)<br>0 | 0 / 11 (0.00%)<br>0 | 1 / 10 (10.00%)<br>1 |
| Skin and subcutaneous tissue disorders           |                     |                     |                      |
| Alopecia   |                     |                     |                      |
| subjects affected / exposed                      | 0 / 41 (0.00%)      | 1 / 11 (9.09%)      | 1 / 10 (10.00%)      |
| occurrences (all)                                | 0                   | 1                   | 1                    |
| Actinic keratosis                                |                     |                     |                      |
| subjects affected / exposed                      | 0 / 41 (0.00%)      | 0 / 11 (0.00%)      | 0 / 10 (0.00%)       |
| occurrences (all)                                | 0                   | 0                   | 0                    |
| Dermatitis acneiform                             |                     |                     |                      |
| subjects affected / exposed                      | 0 / 41 (0.00%)      | 1 / 11 (9.09%)      | 0 / 10 (0.00%)       |
| occurrences (all)                                | 0                   | 1                   | 0                    |
| Dry skin   |                     |                     |                      |
| subjects affected / exposed                      | 7 / 41 (17.07%)     | 1 / 11 (9.09%)      | 0 / 10 (0.00%)       |
| occurrences (all)                                | 7                   | 1                   | 0                    |
| Dermatitis exfoliative generalised               |                     |                     |                      |
| subjects affected / exposed                      | 0 / 41 (0.00%)      | 0 / 11 (0.00%)      | 0 / 10 (0.00%)       |
| occurrences (all)                                | 0                   | 0                   | 0                    |
| Hyperhidrosis                                    |                     |                     |                      |
| subjects affected / exposed                      | 3 / 41 (7.32%)      | 0 / 11 (0.00%)      | 0 / 10 (0.00%)       |
| occurrences (all)                                | 3                   | 0                   | 0                    |
| Eczema nummular                                  |                     |                     |                      |
| subjects affected / exposed                      | 0 / 41 (0.00%)      | 0 / 11 (0.00%)      | 0 / 10 (0.00%)       |
| occurrences (all)                                | 0                   | 0                   | 0                    |
| Lichenoid keratosis                              |                     |                     |                      |
| subjects affected / exposed                      | 0 / 41 (0.00%)      | 0 / 11 (0.00%)      | 0 / 10 (0.00%)       |
| occurrences (all)                                | 0                   | 0                   | 0                    |
| Livedo reticularis                               |                     |                     |                      |
| subjects affected / exposed                      | 0 / 41 (0.00%)      | 0 / 11 (0.00%)      | 0 / 10 (0.00%)       |
| occurrences (all)                                | 0                   | 0                   | 0                    |
| Pruritus   |                     |                     |                      |
| subjects affected / exposed                      | 11 / 41 (26.83%)    | 8 / 11 (72.73%)     | 3 / 10 (30.00%)      |
| occurrences (all)                                | 16                  | 8                   | 3                    |
| Rash   |                     |                     |                      |
| subjects affected / exposed                      | 11 / 41 (26.83%)    | 5 / 11 (45.45%)     | 3 / 10 (30.00%)      |
| occurrences (all)                                | 11                  | 6                   | 6                    |

|   |                      |                      |                      |
|---|----------------------|----------------------|----------------------|
| Rash erythematous<br>subjects affected / exposed<br>occurrences (all)     | 0 / 41 (0.00%)<br>0  | 0 / 11 (0.00%)<br>0  | 0 / 10 (0.00%)<br>0  |
| Rash maculo-papular<br>subjects affected / exposed<br>occurrences (all)   | 5 / 41 (12.20%)<br>6 | 2 / 11 (18.18%)<br>2 | 4 / 10 (40.00%)<br>5 |
| Rash papular<br>subjects affected / exposed<br>occurrences (all)          | 1 / 41 (2.44%)<br>1  | 0 / 11 (0.00%)<br>0  | 0 / 10 (0.00%)<br>0  |
| Rash pruritic<br>subjects affected / exposed<br>occurrences (all)         | 1 / 41 (2.44%)<br>2  | 1 / 11 (9.09%)<br>3  | 1 / 10 (10.00%)<br>1 |
| Scab<br>subjects affected / exposed<br>occurrences (all)                  | 0 / 41 (0.00%)<br>0  | 0 / 11 (0.00%)<br>0  | 0 / 10 (0.00%)<br>0  |
| Skin hypopigmentation<br>subjects affected / exposed<br>occurrences (all) | 1 / 41 (2.44%)<br>1  | 1 / 11 (9.09%)<br>1  | 1 / 10 (10.00%)<br>1 |
| Vitiligo<br>subjects affected / exposed<br>occurrences (all)              | 4 / 41 (9.76%)<br>4  | 2 / 11 (18.18%)<br>2 | 1 / 10 (10.00%)<br>1 |
| Erythema<br>subjects affected / exposed<br>occurrences (all)              | 2 / 41 (4.88%)<br>2  | 1 / 11 (9.09%)<br>1  | 0 / 10 (0.00%)<br>0  |
| Night sweats<br>subjects affected / exposed<br>occurrences (all)          | 2 / 41 (4.88%)<br>2  | 1 / 11 (9.09%)<br>1  | 0 / 10 (0.00%)<br>0  |
| Scar pain<br>subjects affected / exposed<br>occurrences (all)             | 0 / 41 (0.00%)<br>0  | 1 / 11 (9.09%)<br>1  | 0 / 10 (0.00%)<br>0  |
| Skin ulcer<br>subjects affected / exposed<br>occurrences (all)            | 0 / 41 (0.00%)<br>0  | 1 / 11 (9.09%)<br>1  | 0 / 10 (0.00%)<br>0  |
| Facial wasting<br>subjects affected / exposed<br>occurrences (all)        | 0 / 41 (0.00%)<br>0  | 0 / 11 (0.00%)<br>0  | 0 / 10 (0.00%)<br>0  |

|                             |                |                 |                 |
|-----------------------------|----------------|-----------------|-----------------|
| Renal and urinary disorders |                |                 |                 |
| Chromaturia                 |                |                 |                 |
| subjects affected / exposed | 1 / 41 (2.44%) | 0 / 11 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)           | 1              | 0               | 0               |
| Acute kidney injury         |                |                 |                 |
| subjects affected / exposed | 0 / 41 (0.00%) | 0 / 11 (0.00%)  | 1 / 10 (10.00%) |
| occurrences (all)           | 0              | 0               | 1               |
| Dysuria                     |                |                 |                 |
| subjects affected / exposed | 3 / 41 (7.32%) | 1 / 11 (9.09%)  | 2 / 10 (20.00%) |
| occurrences (all)           | 4              | 1               | 2               |
| Pollakiuria                 |                |                 |                 |
| subjects affected / exposed | 0 / 41 (0.00%) | 0 / 11 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)           | 0              | 0               | 0               |
| Haematuria                  |                |                 |                 |
| subjects affected / exposed | 2 / 41 (4.88%) | 1 / 11 (9.09%)  | 0 / 10 (0.00%)  |
| occurrences (all)           | 3              | 1               | 0               |
| Nocturia                    |                |                 |                 |
| subjects affected / exposed | 0 / 41 (0.00%) | 1 / 11 (9.09%)  | 0 / 10 (0.00%)  |
| occurrences (all)           | 0              | 1               | 0               |
| Polyuria                    |                |                 |                 |
| subjects affected / exposed | 0 / 41 (0.00%) | 0 / 11 (0.00%)  | 1 / 10 (10.00%) |
| occurrences (all)           | 0              | 0               | 1               |
| Urinary hesitation          |                |                 |                 |
| subjects affected / exposed | 0 / 41 (0.00%) | 0 / 11 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)           | 0              | 0               | 0               |
| Urinary incontinence        |                |                 |                 |
| subjects affected / exposed | 0 / 41 (0.00%) | 1 / 11 (9.09%)  | 0 / 10 (0.00%)  |
| occurrences (all)           | 0              | 1               | 0               |
| Endocrine disorders         |                |                 |                 |
| Adrenal insufficiency       |                |                 |                 |
| subjects affected / exposed | 0 / 41 (0.00%) | 2 / 11 (18.18%) | 0 / 10 (0.00%)  |
| occurrences (all)           | 0              | 2               | 0               |
| Endocrine disorder          |                |                 |                 |
| subjects affected / exposed | 0 / 41 (0.00%) | 0 / 11 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)           | 0              | 0               | 0               |
| Hyperthyroidism             |                |                 |                 |

|   |                  |                 |                 |
|---|------------------|-----------------|-----------------|
| subjects affected / exposed                     | 1 / 41 (2.44%)   | 3 / 11 (27.27%) | 3 / 10 (30.00%) |
| occurrences (all)                               | 1                | 3               | 3               |
| Hypophysitis                                    |                  |                 |                 |
| subjects affected / exposed                     | 0 / 41 (0.00%)   | 0 / 11 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)                               | 0                | 0               | 0               |
| Hypothyroidism                                  |                  |                 |                 |
| subjects affected / exposed                     | 5 / 41 (12.20%)  | 1 / 11 (9.09%)  | 3 / 10 (30.00%) |
| occurrences (all)                               | 6                | 1               | 3               |
| Thyroiditis                                     |                  |                 |                 |
| subjects affected / exposed                     | 0 / 41 (0.00%)   | 0 / 11 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)                               | 0                | 0               | 0               |
| Musculoskeletal and connective tissue disorders |                  |                 |                 |
| Arthralgia                                      |                  |                 |                 |
| subjects affected / exposed                     | 8 / 41 (19.51%)  | 2 / 11 (18.18%) | 3 / 10 (30.00%) |
| occurrences (all)                               | 13               | 2               | 4               |
| Arthritis                                       |                  |                 |                 |
| subjects affected / exposed                     | 0 / 41 (0.00%)   | 0 / 11 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)                               | 0                | 0               | 0               |
| Back pain                                       |                  |                 |                 |
| subjects affected / exposed                     | 11 / 41 (26.83%) | 1 / 11 (9.09%)  | 1 / 10 (10.00%) |
| occurrences (all)                               | 13               | 1               | 1               |
| Bone pain                                       |                  |                 |                 |
| subjects affected / exposed                     | 0 / 41 (0.00%)   | 0 / 11 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)                               | 0                | 0               | 0               |
| Flank pain                                      |                  |                 |                 |
| subjects affected / exposed                     | 2 / 41 (4.88%)   | 0 / 11 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)                               | 3                | 0               | 0               |
| Joint range of motion decreased                 |                  |                 |                 |
| subjects affected / exposed                     | 0 / 41 (0.00%)   | 0 / 11 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)                               | 0                | 0               | 0               |
| Muscle spasms                                   |                  |                 |                 |
| subjects affected / exposed                     | 0 / 41 (0.00%)   | 0 / 11 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)                               | 0                | 0               | 0               |
| Musculoskeletal pain                            |                  |                 |                 |

|                             |                 |                 |                 |
|-----------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed | 4 / 41 (9.76%)  | 0 / 11 (0.00%)  | 1 / 10 (10.00%) |
| occurrences (all)           | 4               | 0               | 1               |
| Muscular weakness           |                 |                 |                 |
| subjects affected / exposed | 3 / 41 (7.32%)  | 1 / 11 (9.09%)  | 1 / 10 (10.00%) |
| occurrences (all)           | 3               | 1               | 1               |
| Neck pain                   |                 |                 |                 |
| subjects affected / exposed | 1 / 41 (2.44%)  | 1 / 11 (9.09%)  | 0 / 10 (0.00%)  |
| occurrences (all)           | 1               | 1               | 0               |
| Myalgia                     |                 |                 |                 |
| subjects affected / exposed | 2 / 41 (4.88%)  | 2 / 11 (18.18%) | 1 / 10 (10.00%) |
| occurrences (all)           | 2               | 2               | 1               |
| Pain in extremity           |                 |                 |                 |
| subjects affected / exposed | 7 / 41 (17.07%) | 0 / 11 (0.00%)  | 1 / 10 (10.00%) |
| occurrences (all)           | 8               | 0               | 1               |
| Pain in jaw                 |                 |                 |                 |
| subjects affected / exposed | 0 / 41 (0.00%)  | 0 / 11 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)           | 0               | 0               | 0               |
| Musculoskeletal stiffness   |                 |                 |                 |
| subjects affected / exposed | 0 / 41 (0.00%)  | 1 / 11 (9.09%)  | 0 / 10 (0.00%)  |
| occurrences (all)           | 0               | 1               | 0               |
| Infections and infestations |                 |                 |                 |
| Candida infection           |                 |                 |                 |
| subjects affected / exposed | 1 / 41 (2.44%)  | 0 / 11 (0.00%)  | 2 / 10 (20.00%) |
| occurrences (all)           | 1               | 0               | 2               |
| Cellulitis                  |                 |                 |                 |
| subjects affected / exposed | 0 / 41 (0.00%)  | 0 / 11 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)           | 0               | 0               | 0               |
| Conjunctivitis              |                 |                 |                 |
| subjects affected / exposed | 1 / 41 (2.44%)  | 0 / 11 (0.00%)  | 1 / 10 (10.00%) |
| occurrences (all)           | 1               | 0               | 1               |
| Influenza                   |                 |                 |                 |
| subjects affected / exposed | 0 / 41 (0.00%)  | 0 / 11 (0.00%)  | 1 / 10 (10.00%) |
| occurrences (all)           | 0               | 0               | 1               |
| Cytomegalovirus infection   |                 |                 |                 |
| subjects affected / exposed | 0 / 41 (0.00%)  | 0 / 11 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)           | 0               | 0               | 0               |

|                                   |                |                |                 |
|-----------------------------------|----------------|----------------|-----------------|
| Pneumonia                         |                |                |                 |
| subjects affected / exposed       | 2 / 41 (4.88%) | 1 / 11 (9.09%) | 0 / 10 (0.00%)  |
| occurrences (all)                 | 2              | 1              | 0               |
| Nasopharyngitis                   |                |                |                 |
| subjects affected / exposed       | 3 / 41 (7.32%) | 1 / 11 (9.09%) | 2 / 10 (20.00%) |
| occurrences (all)                 | 4              | 1              | 3               |
| Rash pustular                     |                |                |                 |
| subjects affected / exposed       | 0 / 41 (0.00%) | 0 / 11 (0.00%) | 0 / 10 (0.00%)  |
| occurrences (all)                 | 0              | 0              | 0               |
| Respiratory tract infection       |                |                |                 |
| subjects affected / exposed       | 0 / 41 (0.00%) | 1 / 11 (9.09%) | 0 / 10 (0.00%)  |
| occurrences (all)                 | 0              | 1              | 0               |
| Rhinitis                          |                |                |                 |
| subjects affected / exposed       | 1 / 41 (2.44%) | 0 / 11 (0.00%) | 0 / 10 (0.00%)  |
| occurrences (all)                 | 1              | 0              | 0               |
| Sepsis                            |                |                |                 |
| subjects affected / exposed       | 0 / 41 (0.00%) | 1 / 11 (9.09%) | 1 / 10 (10.00%) |
| occurrences (all)                 | 0              | 1              | 1               |
| Sinusitis                         |                |                |                 |
| subjects affected / exposed       | 2 / 41 (4.88%) | 0 / 11 (0.00%) | 2 / 10 (20.00%) |
| occurrences (all)                 | 5              | 0              | 2               |
| Skin infection                    |                |                |                 |
| subjects affected / exposed       | 3 / 41 (7.32%) | 0 / 11 (0.00%) | 0 / 10 (0.00%)  |
| occurrences (all)                 | 3              | 0              | 0               |
| Upper respiratory tract infection |                |                |                 |
| subjects affected / exposed       | 4 / 41 (9.76%) | 1 / 11 (9.09%) | 2 / 10 (20.00%) |
| occurrences (all)                 | 4              | 1              | 2               |
| Urinary tract infection           |                |                |                 |
| subjects affected / exposed       | 2 / 41 (4.88%) | 1 / 11 (9.09%) | 1 / 10 (10.00%) |
| occurrences (all)                 | 3              | 1              | 1               |
| Fungal skin infection             |                |                |                 |
| subjects affected / exposed       | 0 / 41 (0.00%) | 0 / 11 (0.00%) | 1 / 10 (10.00%) |
| occurrences (all)                 | 0              | 0              | 1               |
| Hordeolum                         |                |                |                 |
| subjects affected / exposed       | 0 / 41 (0.00%) | 1 / 11 (9.09%) | 0 / 10 (0.00%)  |
| occurrences (all)                 | 0              | 1              | 0               |

|                                    |                  |                 |                 |
|------------------------------------|------------------|-----------------|-----------------|
| Infected skin ulcer                |                  |                 |                 |
| subjects affected / exposed        | 0 / 41 (0.00%)   | 0 / 11 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)                  | 0                | 0               | 0               |
| Laryngitis                         |                  |                 |                 |
| subjects affected / exposed        | 0 / 41 (0.00%)   | 0 / 11 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)                  | 0                | 0               | 0               |
| Onychomycosis                      |                  |                 |                 |
| subjects affected / exposed        | 0 / 41 (0.00%)   | 0 / 11 (0.00%)  | 1 / 10 (10.00%) |
| occurrences (all)                  | 0                | 0               | 1               |
| Oral candidiasis                   |                  |                 |                 |
| subjects affected / exposed        | 0 / 41 (0.00%)   | 1 / 11 (9.09%)  | 0 / 10 (0.00%)  |
| occurrences (all)                  | 0                | 1               | 0               |
| Oral herpes                        |                  |                 |                 |
| subjects affected / exposed        | 2 / 41 (4.88%)   | 0 / 11 (0.00%)  | 1 / 10 (10.00%) |
| occurrences (all)                  | 2                | 0               | 1               |
| Pyuria                             |                  |                 |                 |
| subjects affected / exposed        | 0 / 41 (0.00%)   | 1 / 11 (9.09%)  | 0 / 10 (0.00%)  |
| occurrences (all)                  | 0                | 1               | 0               |
| Staphylococcal infection           |                  |                 |                 |
| subjects affected / exposed        | 0 / 41 (0.00%)   | 0 / 11 (0.00%)  | 1 / 10 (10.00%) |
| occurrences (all)                  | 0                | 0               | 1               |
| Herpes zoster                      |                  |                 |                 |
| subjects affected / exposed        | 0 / 41 (0.00%)   | 0 / 11 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)                  | 0                | 0               | 0               |
| Metabolism and nutrition disorders |                  |                 |                 |
| Decreased appetite                 |                  |                 |                 |
| subjects affected / exposed        | 10 / 41 (24.39%) | 5 / 11 (45.45%) | 3 / 10 (30.00%) |
| occurrences (all)                  | 11               | 6               | 3               |
| Dehydration                        |                  |                 |                 |
| subjects affected / exposed        | 2 / 41 (4.88%)   | 3 / 11 (27.27%) | 1 / 10 (10.00%) |
| occurrences (all)                  | 2                | 3               | 2               |
| Hypercalcaemia                     |                  |                 |                 |
| subjects affected / exposed        | 0 / 41 (0.00%)   | 0 / 11 (0.00%)  | 1 / 10 (10.00%) |
| occurrences (all)                  | 0                | 0               | 1               |
| Hyperglycaemia                     |                  |                 |                 |

|                             |                |                 |                 |
|-----------------------------|----------------|-----------------|-----------------|
| subjects affected / exposed | 4 / 41 (9.76%) | 2 / 11 (18.18%) | 0 / 10 (0.00%)  |
| occurrences (all)           | 7              | 2               | 0               |
| Hyperuricaemia              |                |                 |                 |
| subjects affected / exposed | 0 / 41 (0.00%) | 0 / 11 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)           | 0              | 0               | 0               |
| Hypoalbuminaemia            |                |                 |                 |
| subjects affected / exposed | 0 / 41 (0.00%) | 1 / 11 (9.09%)  | 0 / 10 (0.00%)  |
| occurrences (all)           | 0              | 1               | 0               |
| Hypoglycaemia               |                |                 |                 |
| subjects affected / exposed | 0 / 41 (0.00%) | 0 / 11 (0.00%)  | 0 / 10 (0.00%)  |
| occurrences (all)           | 0              | 0               | 0               |
| Hypokalaemia                |                |                 |                 |
| subjects affected / exposed | 1 / 41 (2.44%) | 2 / 11 (18.18%) | 2 / 10 (20.00%) |
| occurrences (all)           | 1              | 2               | 3               |
| Hypomagnesaemia             |                |                 |                 |
| subjects affected / exposed | 2 / 41 (4.88%) | 0 / 11 (0.00%)  | 1 / 10 (10.00%) |
| occurrences (all)           | 3              | 0               | 1               |
| Hyponatraemia               |                |                 |                 |
| subjects affected / exposed | 3 / 41 (7.32%) | 2 / 11 (18.18%) | 2 / 10 (20.00%) |
| occurrences (all)           | 3              | 2               | 2               |
| Hypophosphataemia           |                |                 |                 |
| subjects affected / exposed | 3 / 41 (7.32%) | 0 / 11 (0.00%)  | 2 / 10 (20.00%) |
| occurrences (all)           | 4              | 0               | 2               |
| Lactic acidosis             |                |                 |                 |
| subjects affected / exposed | 0 / 41 (0.00%) | 0 / 11 (0.00%)  | 1 / 10 (10.00%) |
| occurrences (all)           | 0              | 0               | 1               |
| Malnutrition                |                |                 |                 |
| subjects affected / exposed | 0 / 41 (0.00%) | 0 / 11 (0.00%)  | 1 / 10 (10.00%) |
| occurrences (all)           | 0              | 0               | 1               |
| Diabetes mellitus           |                |                 |                 |
| subjects affected / exposed | 0 / 41 (0.00%) | 1 / 11 (9.09%)  | 0 / 10 (0.00%)  |
| occurrences (all)           | 0              | 1               | 0               |
| Fluid retention             |                |                 |                 |
| subjects affected / exposed | 0 / 41 (0.00%) | 1 / 11 (9.09%)  | 0 / 10 (0.00%)  |
| occurrences (all)           | 0              | 2               | 0               |
| Hyperkalaemia               |                |                 |                 |



|                             |                |                |                 |
|-----------------------------|----------------|----------------|-----------------|
| subjects affected / exposed | 0 / 41 (0.00%) | 0 / 11 (0.00%) | 0 / 10 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0               |
| Hypocalcaemia               |                |                |                 |
| subjects affected / exposed | 0 / 41 (0.00%) | 0 / 11 (0.00%) | 1 / 10 (10.00%) |
| occurrences (all)           | 0              | 0              | 1               |
| Hypophagia                  |                |                |                 |
| subjects affected / exposed | 0 / 41 (0.00%) | 0 / 11 (0.00%) | 0 / 10 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0               |

| <b>Non-serious adverse events</b>                                   | N1 60M + I3 90M,<br>WU | N3 60M PROG       | N1 30M + I3 30M<br>non-BM |
|---|------------------------|-------------------|---------------------------|
| Total subjects affected by non-serious adverse events               |                        |                   |                           |
| subjects affected / exposed   | 6 / 6 (100.00%)        | 44 / 44 (100.00%) | 25 / 25 (100.00%)         |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                        |                   |                           |
| Malignant neoplasm progression                                      |                        |                   |                           |
| subjects affected / exposed   | 0 / 6 (0.00%)          | 0 / 44 (0.00%)    | 0 / 25 (0.00%)            |
| occurrences (all)   | 0                      | 0                 | 0                         |
| Tumour pain   |                        |                   |                           |
| subjects affected / exposed   | 0 / 6 (0.00%)          | 2 / 44 (4.55%)    | 2 / 25 (8.00%)            |
| occurrences (all)   | 0                      | 2                 | 2                         |
| Tumour embolism   |                        |                   |                           |
| subjects affected / exposed   | 0 / 6 (0.00%)          | 0 / 44 (0.00%)    | 0 / 25 (0.00%)            |
| occurrences (all)   | 0                      | 0                 | 0                         |
| Oncologic complication  |                        |                   |                           |
| subjects affected / exposed   | 0 / 6 (0.00%)          | 0 / 44 (0.00%)    | 0 / 25 (0.00%)            |
| occurrences (all)   | 0                      | 0                 | 0                         |
| Vascular disorders  |                        |                   |                           |
| Embolism  |                        |                   |                           |
| subjects affected / exposed   | 1 / 6 (16.67%)         | 0 / 44 (0.00%)    | 0 / 25 (0.00%)            |
| occurrences (all)   | 1                      | 0                 | 0                         |
| Flushing  |                        |                   |                           |
| subjects affected / exposed   | 0 / 6 (0.00%)          | 2 / 44 (4.55%)    | 0 / 25 (0.00%)            |
| occurrences (all)   | 0                      | 2                 | 0                         |
| Hypertension  |                        |                   |                           |
| subjects affected / exposed   | 0 / 6 (0.00%)          | 1 / 44 (2.27%)    | 1 / 25 (4.00%)            |
| occurrences (all)   | 0                      | 1                 | 1                         |
| Hypotension   |                        |                   |                           |

|  |                |                  |                  |
|--|----------------|------------------|------------------|
| subjects affected / exposed                          | 1 / 6 (16.67%) | 0 / 44 (0.00%)   | 2 / 25 (8.00%)   |
| occurrences (all)                                    | 2              | 0                | 2                |
| Lymphoedema  |                |                  |                  |
| subjects affected / exposed                          | 0 / 6 (0.00%)  | 0 / 44 (0.00%)   | 0 / 25 (0.00%)   |
| occurrences (all)                                    | 0              | 0                | 0                |
| Hot flush  |                |                  |                  |
| subjects affected / exposed                          | 0 / 6 (0.00%)  | 0 / 44 (0.00%)   | 1 / 25 (4.00%)   |
| occurrences (all)                                    | 0              | 0                | 1                |
| Orthostatic hypotension                              |                |                  |                  |
| subjects affected / exposed                          | 0 / 6 (0.00%)  | 0 / 44 (0.00%)   | 0 / 25 (0.00%)   |
| occurrences (all)                                    | 0              | 0                | 0                |
| General disorders and administration site conditions |                |                  |                  |
| Asthenia   |                |                  |                  |
| subjects affected / exposed                          | 1 / 6 (16.67%) | 1 / 44 (2.27%)   | 3 / 25 (12.00%)  |
| occurrences (all)                                    | 1              | 1                | 3                |
| Chest pain   |                |                  |                  |
| subjects affected / exposed                          | 0 / 6 (0.00%)  | 1 / 44 (2.27%)   | 1 / 25 (4.00%)   |
| occurrences (all)                                    | 0              | 1                | 1                |
| Chills   |                |                  |                  |
| subjects affected / exposed                          | 1 / 6 (16.67%) | 4 / 44 (9.09%)   | 3 / 25 (12.00%)  |
| occurrences (all)                                    | 2              | 5                | 4                |
| Fatigue  |                |                  |                  |
| subjects affected / exposed                          | 4 / 6 (66.67%) | 29 / 44 (65.91%) | 13 / 25 (52.00%) |
| occurrences (all)                                    | 5              | 38               | 19               |
| Hernia pain  |                |                  |                  |
| subjects affected / exposed                          | 0 / 6 (0.00%)  | 0 / 44 (0.00%)   | 0 / 25 (0.00%)   |
| occurrences (all)                                    | 0              | 0                | 0                |
| Influenza like illness                               |                |                  |                  |
| subjects affected / exposed                          | 1 / 6 (16.67%) | 3 / 44 (6.82%)   | 3 / 25 (12.00%)  |
| occurrences (all)                                    | 1              | 3                | 3                |
| Localised oedema                                     |                |                  |                  |
| subjects affected / exposed                          | 1 / 6 (16.67%) | 0 / 44 (0.00%)   | 0 / 25 (0.00%)   |
| occurrences (all)                                    | 1              | 0                | 0                |
| Malaise  |                |                  |                  |

|                                    |                |                  |                 |
|------------------------------------|----------------|------------------|-----------------|
| subjects affected / exposed        | 2 / 6 (33.33%) | 1 / 44 (2.27%)   | 2 / 25 (8.00%)  |
| occurrences (all)                  | 2              | 1                | 2               |
| Mucosal inflammation               |                |                  |                 |
| subjects affected / exposed        | 0 / 6 (0.00%)  | 0 / 44 (0.00%)   | 2 / 25 (8.00%)  |
| occurrences (all)                  | 0              | 0                | 2               |
| Non-cardiac chest pain             |                |                  |                 |
| subjects affected / exposed        | 0 / 6 (0.00%)  | 0 / 44 (0.00%)   | 0 / 25 (0.00%)  |
| occurrences (all)                  | 0              | 0                | 0               |
| Oedema peripheral                  |                |                  |                 |
| subjects affected / exposed        | 2 / 6 (33.33%) | 6 / 44 (13.64%)  | 6 / 25 (24.00%) |
| occurrences (all)                  | 2              | 6                | 8               |
| Pain                               |                |                  |                 |
| subjects affected / exposed        | 1 / 6 (16.67%) | 11 / 44 (25.00%) | 1 / 25 (4.00%)  |
| occurrences (all)                  | 1              | 11               | 1               |
| Peripheral swelling                |                |                  |                 |
| subjects affected / exposed        | 0 / 6 (0.00%)  | 0 / 44 (0.00%)   | 0 / 25 (0.00%)  |
| occurrences (all)                  | 0              | 0                | 0               |
| Pyrexia                            |                |                  |                 |
| subjects affected / exposed        | 3 / 6 (50.00%) | 9 / 44 (20.45%)  | 9 / 25 (36.00%) |
| occurrences (all)                  | 6              | 17               | 10              |
| Temperature intolerance            |                |                  |                 |
| subjects affected / exposed        | 0 / 6 (0.00%)  | 0 / 44 (0.00%)   | 0 / 25 (0.00%)  |
| occurrences (all)                  | 0              | 0                | 0               |
| Decreased activity                 |                |                  |                 |
| subjects affected / exposed        | 0 / 6 (0.00%)  | 0 / 44 (0.00%)   | 0 / 25 (0.00%)  |
| occurrences (all)                  | 0              | 0                | 0               |
| Feeling cold                       |                |                  |                 |
| subjects affected / exposed        | 0 / 6 (0.00%)  | 0 / 44 (0.00%)   | 0 / 25 (0.00%)  |
| occurrences (all)                  | 0              | 0                | 0               |
| Gait disturbance                   |                |                  |                 |
| subjects affected / exposed        | 0 / 6 (0.00%)  | 0 / 44 (0.00%)   | 0 / 25 (0.00%)  |
| occurrences (all)                  | 0              | 0                | 0               |
| Feeling of body temperature change |                |                  |                 |
| subjects affected / exposed        | 0 / 6 (0.00%)  | 0 / 44 (0.00%)   | 0 / 25 (0.00%)  |
| occurrences (all)                  | 0              | 0                | 0               |
| Inflammation                       |                |                  |                 |

|   |                |                  |                 |
|---|----------------|------------------|-----------------|
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 44 (0.00%)   | 0 / 25 (0.00%)  |
| occurrences (all)                               | 0              | 0                | 0               |
| Physical deconditioning                         |                |                  |                 |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 44 (0.00%)   | 1 / 25 (4.00%)  |
| occurrences (all)                               | 0              | 0                | 1               |
| Axillary pain                                   |                |                  |                 |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 1 / 44 (2.27%)   | 0 / 25 (0.00%)  |
| occurrences (all)                               | 0              | 1                | 0               |
| Immune system disorders                         |                |                  |                 |
| Drug hypersensitivity                           |                |                  |                 |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 44 (0.00%)   | 0 / 25 (0.00%)  |
| occurrences (all)                               | 0              | 0                | 0               |
| Hypersensitivity                                |                |                  |                 |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 1 / 44 (2.27%)   | 0 / 25 (0.00%)  |
| occurrences (all)                               | 0              | 1                | 0               |
| Reproductive system and breast disorders        |                |                  |                 |
| Nipple pain                                     |                |                  |                 |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 44 (0.00%)   | 0 / 25 (0.00%)  |
| occurrences (all)                               | 0              | 0                | 0               |
| Spermatic cord haemorrhage                      |                |                  |                 |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 44 (0.00%)   | 0 / 25 (0.00%)  |
| occurrences (all)                               | 0              | 0                | 0               |
| Genital rash                                    |                |                  |                 |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 44 (0.00%)   | 0 / 25 (0.00%)  |
| occurrences (all)                               | 0              | 0                | 0               |
| Scrotal swelling                                |                |                  |                 |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 44 (0.00%)   | 0 / 25 (0.00%)  |
| occurrences (all)                               | 0              | 0                | 0               |
| Respiratory, thoracic and mediastinal disorders |                |                  |                 |
| Bronchial obstruction                           |                |                  |                 |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 44 (0.00%)   | 0 / 25 (0.00%)  |
| occurrences (all)                               | 0              | 0                | 0               |
| Cough   |                |                  |                 |
| subjects affected / exposed                     | 2 / 6 (33.33%) | 13 / 44 (29.55%) | 4 / 25 (16.00%) |
| occurrences (all)                               | 2              | 20               | 6               |
| Dyspnoea  |                |                  |                 |

|                             |                |                 |                 |
|-----------------------------|----------------|-----------------|-----------------|
| subjects affected / exposed | 3 / 6 (50.00%) | 7 / 44 (15.91%) | 5 / 25 (20.00%) |
| occurrences (all)           | 3              | 9               | 6               |
| Hypoxia                     |                |                 |                 |
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 44 (0.00%)  | 0 / 25 (0.00%)  |
| occurrences (all)           | 0              | 0               | 0               |
| Oropharyngeal pain          |                |                 |                 |
| subjects affected / exposed | 1 / 6 (16.67%) | 2 / 44 (4.55%)  | 1 / 25 (4.00%)  |
| occurrences (all)           | 1              | 2               | 1               |
| Nasal congestion            |                |                 |                 |
| subjects affected / exposed | 1 / 6 (16.67%) | 1 / 44 (2.27%)  | 2 / 25 (8.00%)  |
| occurrences (all)           | 1              | 1               | 2               |
| Pleural effusion            |                |                 |                 |
| subjects affected / exposed | 0 / 6 (0.00%)  | 1 / 44 (2.27%)  | 0 / 25 (0.00%)  |
| occurrences (all)           | 0              | 1               | 0               |
| Pneumonitis                 |                |                 |                 |
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 44 (0.00%)  | 3 / 25 (12.00%) |
| occurrences (all)           | 0              | 0               | 3               |
| Productive cough            |                |                 |                 |
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 44 (0.00%)  | 1 / 25 (4.00%)  |
| occurrences (all)           | 0              | 0               | 1               |
| Rhinitis allergic           |                |                 |                 |
| subjects affected / exposed | 0 / 6 (0.00%)  | 1 / 44 (2.27%)  | 0 / 25 (0.00%)  |
| occurrences (all)           | 0              | 1               | 0               |
| Rhinorrhoea                 |                |                 |                 |
| subjects affected / exposed | 0 / 6 (0.00%)  | 1 / 44 (2.27%)  | 0 / 25 (0.00%)  |
| occurrences (all)           | 0              | 1               | 0               |
| Upper-airway cough syndrome |                |                 |                 |
| subjects affected / exposed | 0 / 6 (0.00%)  | 4 / 44 (9.09%)  | 0 / 25 (0.00%)  |
| occurrences (all)           | 0              | 4               | 0               |
| Dysphonia                   |                |                 |                 |
| subjects affected / exposed | 0 / 6 (0.00%)  | 1 / 44 (2.27%)  | 1 / 25 (4.00%)  |
| occurrences (all)           | 0              | 1               | 1               |
| Dyspnoea exertional         |                |                 |                 |
| subjects affected / exposed | 0 / 6 (0.00%)  | 2 / 44 (4.55%)  | 1 / 25 (4.00%)  |
| occurrences (all)           | 0              | 2               | 1               |
| Epistaxis                   |                |                 |                 |

|                              |                |                 |                |
|------------------------------|----------------|-----------------|----------------|
| subjects affected / exposed  | 0 / 6 (0.00%)  | 0 / 44 (0.00%)  | 0 / 25 (0.00%) |
| occurrences (all)            | 0              | 0               | 0              |
| Haemoptysis                  |                |                 |                |
| subjects affected / exposed  | 0 / 6 (0.00%)  | 2 / 44 (4.55%)  | 0 / 25 (0.00%) |
| occurrences (all)            | 0              | 2               | 0              |
| Hiccups                      |                |                 |                |
| subjects affected / exposed  | 1 / 6 (16.67%) | 2 / 44 (4.55%)  | 0 / 25 (0.00%) |
| occurrences (all)            | 1              | 2               | 0              |
| Pulmonary embolism           |                |                 |                |
| subjects affected / exposed  | 0 / 6 (0.00%)  | 0 / 44 (0.00%)  | 1 / 25 (4.00%) |
| occurrences (all)            | 0              | 0               | 1              |
| Respiratory failure          |                |                 |                |
| subjects affected / exposed  | 1 / 6 (16.67%) | 0 / 44 (0.00%)  | 0 / 25 (0.00%) |
| occurrences (all)            | 1              | 0               | 0              |
| Respiratory tract congestion |                |                 |                |
| subjects affected / exposed  | 0 / 6 (0.00%)  | 0 / 44 (0.00%)  | 0 / 25 (0.00%) |
| occurrences (all)            | 0              | 0               | 0              |
| Psychiatric disorders        |                |                 |                |
| Confusional state            |                |                 |                |
| subjects affected / exposed  | 0 / 6 (0.00%)  | 0 / 44 (0.00%)  | 1 / 25 (4.00%) |
| occurrences (all)            | 0              | 0               | 1              |
| Anxiety                      |                |                 |                |
| subjects affected / exposed  | 0 / 6 (0.00%)  | 4 / 44 (9.09%)  | 0 / 25 (0.00%) |
| occurrences (all)            | 0              | 5               | 0              |
| Depression                   |                |                 |                |
| subjects affected / exposed  | 0 / 6 (0.00%)  | 1 / 44 (2.27%)  | 0 / 25 (0.00%) |
| occurrences (all)            | 0              | 1               | 0              |
| Insomnia                     |                |                 |                |
| subjects affected / exposed  | 2 / 6 (33.33%) | 5 / 44 (11.36%) | 2 / 25 (8.00%) |
| occurrences (all)            | 2              | 6               | 2              |
| Sleep disorder               |                |                 |                |
| subjects affected / exposed  | 0 / 6 (0.00%)  | 1 / 44 (2.27%)  | 0 / 25 (0.00%) |
| occurrences (all)            | 0              | 1               | 0              |
| Depressed mood               |                |                 |                |
| subjects affected / exposed  | 0 / 6 (0.00%)  | 0 / 44 (0.00%)  | 0 / 25 (0.00%) |
| occurrences (all)            | 0              | 0               | 0              |

|   |                |                |                 |
|---|----------------|----------------|-----------------|
| Disorientation                                  |                |                |                 |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 44 (0.00%) | 0 / 25 (0.00%)  |
| occurrences (all)                               | 0              | 0              | 0               |
| Irritability                                    |                |                |                 |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 44 (0.00%) | 0 / 25 (0.00%)  |
| occurrences (all)                               | 0              | 0              | 0               |
| Hallucination                                   |                |                |                 |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 44 (0.00%) | 0 / 25 (0.00%)  |
| occurrences (all)                               | 0              | 0              | 0               |
| Mental status changes                           |                |                |                 |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 44 (0.00%) | 0 / 25 (0.00%)  |
| occurrences (all)                               | 0              | 0              | 0               |
| Investigations                                  |                |                |                 |
| Activated partial thromboplastin time prolonged |                |                |                 |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 44 (0.00%) | 0 / 25 (0.00%)  |
| occurrences (all)                               | 0              | 0              | 0               |
| Alanine aminotransferase increased              |                |                |                 |
| subjects affected / exposed                     | 2 / 6 (33.33%) | 2 / 44 (4.55%) | 5 / 25 (20.00%) |
| occurrences (all)                               | 2              | 2              | 6               |
| Amylase increased                               |                |                |                 |
| subjects affected / exposed                     | 1 / 6 (16.67%) | 0 / 44 (0.00%) | 2 / 25 (8.00%)  |
| occurrences (all)                               | 1              | 0              | 2               |
| Aspartate aminotransferase increased            |                |                |                 |
| subjects affected / exposed                     | 2 / 6 (33.33%) | 2 / 44 (4.55%) | 6 / 25 (24.00%) |
| occurrences (all)                               | 2              | 2              | 7               |
| Blood alkaline phosphatase increased            |                |                |                 |
| subjects affected / exposed                     | 2 / 6 (33.33%) | 4 / 44 (9.09%) | 3 / 25 (12.00%) |
| occurrences (all)                               | 2              | 5              | 3               |
| Blood bilirubin increased                       |                |                |                 |
| subjects affected / exposed                     | 1 / 6 (16.67%) | 0 / 44 (0.00%) | 1 / 25 (4.00%)  |
| occurrences (all)                               | 1              | 0              | 1               |
| Blood creatinine increased                      |                |                |                 |
| subjects affected / exposed                     | 1 / 6 (16.67%) | 2 / 44 (4.55%) | 1 / 25 (4.00%)  |
| occurrences (all)                               | 1              | 2              | 1               |
| Blood thyroid stimulating hormone decreased     |                |                |                 |

|   |                |                 |                 |
|---|----------------|-----------------|-----------------|
| subjects affected / exposed                 | 0 / 6 (0.00%)  | 0 / 44 (0.00%)  | 0 / 25 (0.00%)  |
| occurrences (all)                           | 0              | 0               | 0               |
| Blood thyroid stimulating hormone increased |                |                 |                 |
| subjects affected / exposed                 | 0 / 6 (0.00%)  | 1 / 44 (2.27%)  | 1 / 25 (4.00%)  |
| occurrences (all)                           | 0              | 1               | 1               |
| Cortisol increased                          |                |                 |                 |
| subjects affected / exposed                 | 0 / 6 (0.00%)  | 0 / 44 (0.00%)  | 0 / 25 (0.00%)  |
| occurrences (all)                           | 0              | 0               | 0               |
| Hepatic enzyme increased                    |                |                 |                 |
| subjects affected / exposed                 | 0 / 6 (0.00%)  | 0 / 44 (0.00%)  | 0 / 25 (0.00%)  |
| occurrences (all)                           | 0              | 0               | 0               |
| International normalised ratio increased    |                |                 |                 |
| subjects affected / exposed                 | 0 / 6 (0.00%)  | 0 / 44 (0.00%)  | 0 / 25 (0.00%)  |
| occurrences (all)                           | 0              | 0               | 0               |
| Lipase increased                            |                |                 |                 |
| subjects affected / exposed                 | 2 / 6 (33.33%) | 8 / 44 (18.18%) | 3 / 25 (12.00%) |
| occurrences (all)                           | 2              | 13              | 4               |
| Lymphocyte count decreased                  |                |                 |                 |
| subjects affected / exposed                 | 1 / 6 (16.67%) | 1 / 44 (2.27%)  | 1 / 25 (4.00%)  |
| occurrences (all)                           | 1              | 2               | 1               |
| Platelet count decreased                    |                |                 |                 |
| subjects affected / exposed                 | 0 / 6 (0.00%)  | 0 / 44 (0.00%)  | 2 / 25 (8.00%)  |
| occurrences (all)                           | 0              | 0               | 2               |
| Norovirus test positive                     |                |                 |                 |
| subjects affected / exposed                 | 0 / 6 (0.00%)  | 0 / 44 (0.00%)  | 0 / 25 (0.00%)  |
| occurrences (all)                           | 0              | 0               | 0               |
| Transaminases increased                     |                |                 |                 |
| subjects affected / exposed                 | 0 / 6 (0.00%)  | 0 / 44 (0.00%)  | 2 / 25 (8.00%)  |
| occurrences (all)                           | 0              | 0               | 2               |
| Weight decreased                            |                |                 |                 |
| subjects affected / exposed                 | 2 / 6 (33.33%) | 5 / 44 (11.36%) | 3 / 25 (12.00%) |
| occurrences (all)                           | 3              | 6               | 4               |
| Weight increased                            |                |                 |                 |



|  |               |                |                |
|--|---------------|----------------|----------------|
| subjects affected / exposed                    | 0 / 6 (0.00%) | 1 / 44 (2.27%) | 0 / 25 (0.00%) |
| occurrences (all)                              | 0             | 1              | 0              |
| Blood urea increased                           |               |                |                |
| subjects affected / exposed                    | 0 / 6 (0.00%) | 0 / 44 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all)                              | 0             | 0              | 0              |
| Heart rate increased                           |               |                |                |
| subjects affected / exposed                    | 0 / 6 (0.00%) | 0 / 44 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all)                              | 0             | 0              | 0              |
| Injury, poisoning and procedural complications |               |                |                |
| Contusion                                      |               |                |                |
| subjects affected / exposed                    | 0 / 6 (0.00%) | 2 / 44 (4.55%) | 0 / 25 (0.00%) |
| occurrences (all)                              | 0             | 2              | 0              |
| Infusion related reaction                      |               |                |                |
| subjects affected / exposed                    | 0 / 6 (0.00%) | 2 / 44 (4.55%) | 0 / 25 (0.00%) |
| occurrences (all)                              | 0             | 2              | 0              |
| Limb injury                                    |               |                |                |
| subjects affected / exposed                    | 0 / 6 (0.00%) | 0 / 44 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all)                              | 0             | 0              | 0              |
| Procedural pain                                |               |                |                |
| subjects affected / exposed                    | 0 / 6 (0.00%) | 2 / 44 (4.55%) | 0 / 25 (0.00%) |
| occurrences (all)                              | 0             | 2              | 0              |
| Bone fissure                                   |               |                |                |
| subjects affected / exposed                    | 0 / 6 (0.00%) | 0 / 44 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all)                              | 0             | 0              | 0              |
| Radiation pneumonitis                          |               |                |                |
| subjects affected / exposed                    | 0 / 6 (0.00%) | 0 / 44 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all)                              | 0             | 0              | 0              |
| Fall   |               |                |                |
| subjects affected / exposed                    | 0 / 6 (0.00%) | 1 / 44 (2.27%) | 0 / 25 (0.00%) |
| occurrences (all)                              | 0             | 1              | 0              |
| Cardiac disorders                              |               |                |                |
| Acute coronary syndrome                        |               |                |                |
| subjects affected / exposed                    | 0 / 6 (0.00%) | 0 / 44 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all)                              | 0             | 0              | 0              |
| Angina pectoris                                |               |                |                |

|                                      |                |                 |                |
|--------------------------------------|----------------|-----------------|----------------|
| subjects affected / exposed          | 0 / 6 (0.00%)  | 0 / 44 (0.00%)  | 0 / 25 (0.00%) |
| occurrences (all)                    | 0              | 0               | 0              |
| Palpitations                         |                |                 |                |
| subjects affected / exposed          | 1 / 6 (16.67%) | 1 / 44 (2.27%)  | 2 / 25 (8.00%) |
| occurrences (all)                    | 1              | 3               | 2              |
| Tachycardia                          |                |                 |                |
| subjects affected / exposed          | 2 / 6 (33.33%) | 0 / 44 (0.00%)  | 1 / 25 (4.00%) |
| occurrences (all)                    | 3              | 0               | 1              |
| Cardiac failure congestive           |                |                 |                |
| subjects affected / exposed          | 0 / 6 (0.00%)  | 0 / 44 (0.00%)  | 0 / 25 (0.00%) |
| occurrences (all)                    | 0              | 0               | 0              |
| Atrioventricular block second degree |                |                 |                |
| subjects affected / exposed          | 0 / 6 (0.00%)  | 0 / 44 (0.00%)  | 0 / 25 (0.00%) |
| occurrences (all)                    | 0              | 0               | 0              |
| Nervous system disorders             |                |                 |                |
| Autonomic nervous system imbalance   |                |                 |                |
| subjects affected / exposed          | 0 / 6 (0.00%)  | 0 / 44 (0.00%)  | 1 / 25 (4.00%) |
| occurrences (all)                    | 0              | 0               | 1              |
| Cerebrovascular accident             |                |                 |                |
| subjects affected / exposed          | 0 / 6 (0.00%)  | 0 / 44 (0.00%)  | 0 / 25 (0.00%) |
| occurrences (all)                    | 0              | 0               | 0              |
| Disturbance in attention             |                |                 |                |
| subjects affected / exposed          | 0 / 6 (0.00%)  | 0 / 44 (0.00%)  | 1 / 25 (4.00%) |
| occurrences (all)                    | 0              | 0               | 1              |
| Dizziness                            |                |                 |                |
| subjects affected / exposed          | 2 / 6 (33.33%) | 8 / 44 (18.18%) | 1 / 25 (4.00%) |
| occurrences (all)                    | 5              | 9               | 1              |
| Dysaesthesia                         |                |                 |                |
| subjects affected / exposed          | 0 / 6 (0.00%)  | 0 / 44 (0.00%)  | 0 / 25 (0.00%) |
| occurrences (all)                    | 0              | 0               | 0              |
| Dysarthria                           |                |                 |                |
| subjects affected / exposed          | 0 / 6 (0.00%)  | 0 / 44 (0.00%)  | 0 / 25 (0.00%) |
| occurrences (all)                    | 0              | 0               | 0              |
| Dysgeusia                            |                |                 |                |

|                             |                |                 |                 |
|-----------------------------|----------------|-----------------|-----------------|
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 44 (0.00%)  | 1 / 25 (4.00%)  |
| occurrences (all)           | 1              | 0               | 1               |
| Headache                    |                |                 |                 |
| subjects affected / exposed | 3 / 6 (50.00%) | 9 / 44 (20.45%) | 9 / 25 (36.00%) |
| occurrences (all)           | 6              | 11              | 10              |
| Hemiparesis                 |                |                 |                 |
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 44 (0.00%)  | 0 / 25 (0.00%)  |
| occurrences (all)           | 0              | 0               | 0               |
| Lethargy                    |                |                 |                 |
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 44 (0.00%)  | 0 / 25 (0.00%)  |
| occurrences (all)           | 0              | 0               | 0               |
| Neuropathy peripheral       |                |                 |                 |
| subjects affected / exposed | 0 / 6 (0.00%)  | 3 / 44 (6.82%)  | 1 / 25 (4.00%)  |
| occurrences (all)           | 0              | 3               | 1               |
| Paraesthesia                |                |                 |                 |
| subjects affected / exposed | 0 / 6 (0.00%)  | 1 / 44 (2.27%)  | 0 / 25 (0.00%)  |
| occurrences (all)           | 0              | 1               | 0               |
| Presyncope                  |                |                 |                 |
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 44 (0.00%)  | 1 / 25 (4.00%)  |
| occurrences (all)           | 0              | 0               | 1               |
| Restless legs syndrome      |                |                 |                 |
| subjects affected / exposed | 0 / 6 (0.00%)  | 1 / 44 (2.27%)  | 0 / 25 (0.00%)  |
| occurrences (all)           | 0              | 1               | 0               |
| Seizure                     |                |                 |                 |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 44 (0.00%)  | 0 / 25 (0.00%)  |
| occurrences (all)           | 1              | 0               | 0               |
| Aphasia                     |                |                 |                 |
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 44 (0.00%)  | 0 / 25 (0.00%)  |
| occurrences (all)           | 0              | 0               | 0               |
| Amnesia                     |                |                 |                 |
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 44 (0.00%)  | 0 / 25 (0.00%)  |
| occurrences (all)           | 0              | 0               | 0               |
| Fine motor delay            |                |                 |                 |
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 44 (0.00%)  | 0 / 25 (0.00%)  |
| occurrences (all)           | 0              | 0               | 0               |
| Encephalopathy              |                |                 |                 |

|                                      |                |                 |                 |
|--------------------------------------|----------------|-----------------|-----------------|
| subjects affected / exposed          | 0 / 6 (0.00%)  | 0 / 44 (0.00%)  | 1 / 25 (4.00%)  |
| occurrences (all)                    | 0              | 0               | 1               |
| Hypersomnia                          |                |                 |                 |
| subjects affected / exposed          | 0 / 6 (0.00%)  | 0 / 44 (0.00%)  | 0 / 25 (0.00%)  |
| occurrences (all)                    | 0              | 0               | 0               |
| Hypoaesthesia                        |                |                 |                 |
| subjects affected / exposed          | 0 / 6 (0.00%)  | 2 / 44 (4.55%)  | 1 / 25 (4.00%)  |
| occurrences (all)                    | 0              | 3               | 1               |
| Mental impairment                    |                |                 |                 |
| subjects affected / exposed          | 0 / 6 (0.00%)  | 0 / 44 (0.00%)  | 0 / 25 (0.00%)  |
| occurrences (all)                    | 0              | 0               | 0               |
| Muscle spasticity                    |                |                 |                 |
| subjects affected / exposed          | 0 / 6 (0.00%)  | 0 / 44 (0.00%)  | 0 / 25 (0.00%)  |
| occurrences (all)                    | 0              | 0               | 0               |
| Neurotoxicity                        |                |                 |                 |
| subjects affected / exposed          | 0 / 6 (0.00%)  | 0 / 44 (0.00%)  | 0 / 25 (0.00%)  |
| occurrences (all)                    | 0              | 0               | 0               |
| Somnolence                           |                |                 |                 |
| subjects affected / exposed          | 0 / 6 (0.00%)  | 1 / 44 (2.27%)  | 0 / 25 (0.00%)  |
| occurrences (all)                    | 0              | 1               | 0               |
| Syncope                              |                |                 |                 |
| subjects affected / exposed          | 0 / 6 (0.00%)  | 0 / 44 (0.00%)  | 0 / 25 (0.00%)  |
| occurrences (all)                    | 0              | 0               | 0               |
| Spinal cord compression              |                |                 |                 |
| subjects affected / exposed          | 0 / 6 (0.00%)  | 0 / 44 (0.00%)  | 0 / 25 (0.00%)  |
| occurrences (all)                    | 0              | 0               | 0               |
| Tremor                               |                |                 |                 |
| subjects affected / exposed          | 0 / 6 (0.00%)  | 0 / 44 (0.00%)  | 0 / 25 (0.00%)  |
| occurrences (all)                    | 0              | 0               | 0               |
| Balance disorder                     |                |                 |                 |
| subjects affected / exposed          | 0 / 6 (0.00%)  | 0 / 44 (0.00%)  | 1 / 25 (4.00%)  |
| occurrences (all)                    | 0              | 0               | 1               |
| Blood and lymphatic system disorders |                |                 |                 |
| Anaemia                              |                |                 |                 |
| subjects affected / exposed          | 2 / 6 (33.33%) | 8 / 44 (18.18%) | 5 / 25 (20.00%) |
| occurrences (all)                    | 2              | 9               | 7               |

|   |                     |                     |                     |
|---|---------------------|---------------------|---------------------|
| Haemolytic anaemia<br>subjects affected / exposed<br>occurrences (all)                        | 0 / 6 (0.00%)<br>0  | 0 / 44 (0.00%)<br>0 | 0 / 25 (0.00%)<br>0 |
| Thrombocytopenia<br>subjects affected / exposed<br>occurrences (all)                          | 0 / 6 (0.00%)<br>0  | 1 / 44 (2.27%)<br>3 | 1 / 25 (4.00%)<br>2 |
| Coagulopathy<br>subjects affected / exposed<br>occurrences (all)                              | 0 / 6 (0.00%)<br>0  | 0 / 44 (0.00%)<br>0 | 0 / 25 (0.00%)<br>0 |
| Lymphadenopathy<br>subjects affected / exposed<br>occurrences (all)                           | 0 / 6 (0.00%)<br>0  | 0 / 44 (0.00%)<br>0 | 0 / 25 (0.00%)<br>0 |
| Microcytic anaemia<br>subjects affected / exposed<br>occurrences (all)                        | 0 / 6 (0.00%)<br>0  | 0 / 44 (0.00%)<br>0 | 0 / 25 (0.00%)<br>0 |
| Ear and labyrinth disorders<br>Hypoacusis<br>subjects affected / exposed<br>occurrences (all) | 0 / 6 (0.00%)<br>0  | 1 / 44 (2.27%)<br>1 | 1 / 25 (4.00%)<br>1 |
| Cerumen impaction<br>subjects affected / exposed<br>occurrences (all)                         | 0 / 6 (0.00%)<br>0  | 0 / 44 (0.00%)<br>0 | 0 / 25 (0.00%)<br>0 |
| Eye disorders<br>Dry eye<br>subjects affected / exposed<br>occurrences (all)                  | 0 / 6 (0.00%)<br>0  | 1 / 44 (2.27%)<br>1 | 0 / 25 (0.00%)<br>0 |
| Eye disorder<br>subjects affected / exposed<br>occurrences (all)                              | 0 / 6 (0.00%)<br>0  | 0 / 44 (0.00%)<br>0 | 0 / 25 (0.00%)<br>0 |
| Eye pain<br>subjects affected / exposed<br>occurrences (all)                                  | 1 / 6 (16.67%)<br>1 | 1 / 44 (2.27%)<br>1 | 2 / 25 (8.00%)<br>2 |
| Uveitis<br>subjects affected / exposed<br>occurrences (all)                                   | 0 / 6 (0.00%)<br>0  | 0 / 44 (0.00%)<br>0 | 0 / 25 (0.00%)<br>0 |
| Vision blurred  |                     |                     |                     |

|                             |                |                 |                 |
|-----------------------------|----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 6 (0.00%)  | 3 / 44 (6.82%)  | 3 / 25 (12.00%) |
| occurrences (all)           | 0              | 3               | 3               |
| Visual impairment           |                |                 |                 |
| subjects affected / exposed | 0 / 6 (0.00%)  | 2 / 44 (4.55%)  | 0 / 25 (0.00%)  |
| occurrences (all)           | 0              | 2               | 0               |
| Eye pruritus                |                |                 |                 |
| subjects affected / exposed | 0 / 6 (0.00%)  | 1 / 44 (2.27%)  | 0 / 25 (0.00%)  |
| occurrences (all)           | 0              | 1               | 0               |
| Eye swelling                |                |                 |                 |
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 44 (0.00%)  | 0 / 25 (0.00%)  |
| occurrences (all)           | 0              | 0               | 0               |
| Iridocyclitis               |                |                 |                 |
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 44 (0.00%)  | 0 / 25 (0.00%)  |
| occurrences (all)           | 0              | 0               | 0               |
| Lacrimation increased       |                |                 |                 |
| subjects affected / exposed | 0 / 6 (0.00%)  | 1 / 44 (2.27%)  | 0 / 25 (0.00%)  |
| occurrences (all)           | 0              | 1               | 0               |
| Ocular hyperaemia           |                |                 |                 |
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 44 (0.00%)  | 0 / 25 (0.00%)  |
| occurrences (all)           | 0              | 0               | 0               |
| Conjunctival oedema         |                |                 |                 |
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 44 (0.00%)  | 0 / 25 (0.00%)  |
| occurrences (all)           | 0              | 0               | 0               |
| Gastrointestinal disorders  |                |                 |                 |
| Abdominal discomfort        |                |                 |                 |
| subjects affected / exposed | 0 / 6 (0.00%)  | 1 / 44 (2.27%)  | 0 / 25 (0.00%)  |
| occurrences (all)           | 0              | 1               | 0               |
| Abdominal distension        |                |                 |                 |
| subjects affected / exposed | 0 / 6 (0.00%)  | 3 / 44 (6.82%)  | 1 / 25 (4.00%)  |
| occurrences (all)           | 0              | 3               | 1               |
| Abdominal pain              |                |                 |                 |
| subjects affected / exposed | 3 / 6 (50.00%) | 5 / 44 (11.36%) | 4 / 25 (16.00%) |
| occurrences (all)           | 4              | 5               | 4               |
| Abdominal pain upper        |                |                 |                 |
| subjects affected / exposed | 0 / 6 (0.00%)  | 2 / 44 (4.55%)  | 3 / 25 (12.00%) |
| occurrences (all)           | 0              | 2               | 4               |

|                              |                |                  |                  |
|------------------------------|----------------|------------------|------------------|
| Anal pruritus                |                |                  |                  |
| subjects affected / exposed  | 0 / 6 (0.00%)  | 0 / 44 (0.00%)   | 0 / 25 (0.00%)   |
| occurrences (all)            | 0              | 0                | 0                |
| Colitis                      |                |                  |                  |
| subjects affected / exposed  | 2 / 6 (33.33%) | 1 / 44 (2.27%)   | 0 / 25 (0.00%)   |
| occurrences (all)            | 2              | 1                | 0                |
| Constipation                 |                |                  |                  |
| subjects affected / exposed  | 1 / 6 (16.67%) | 14 / 44 (31.82%) | 1 / 25 (4.00%)   |
| occurrences (all)            | 2              | 18               | 1                |
| Diarrhoea                    |                |                  |                  |
| subjects affected / exposed  | 2 / 6 (33.33%) | 14 / 44 (31.82%) | 9 / 25 (36.00%)  |
| occurrences (all)            | 7              | 30               | 15               |
| Dry mouth                    |                |                  |                  |
| subjects affected / exposed  | 1 / 6 (16.67%) | 6 / 44 (13.64%)  | 2 / 25 (8.00%)   |
| occurrences (all)            | 1              | 6                | 2                |
| Dyspepsia                    |                |                  |                  |
| subjects affected / exposed  | 0 / 6 (0.00%)  | 4 / 44 (9.09%)   | 2 / 25 (8.00%)   |
| occurrences (all)            | 0              | 5                | 5                |
| Dysphagia                    |                |                  |                  |
| subjects affected / exposed  | 0 / 6 (0.00%)  | 0 / 44 (0.00%)   | 0 / 25 (0.00%)   |
| occurrences (all)            | 0              | 0                | 0                |
| Gastritis                    |                |                  |                  |
| subjects affected / exposed  | 0 / 6 (0.00%)  | 0 / 44 (0.00%)   | 1 / 25 (4.00%)   |
| occurrences (all)            | 0              | 0                | 1                |
| Flatulence                   |                |                  |                  |
| subjects affected / exposed  | 1 / 6 (16.67%) | 2 / 44 (4.55%)   | 0 / 25 (0.00%)   |
| occurrences (all)            | 1              | 2                | 0                |
| Gastrointestinal haemorrhage |                |                  |                  |
| subjects affected / exposed  | 0 / 6 (0.00%)  | 0 / 44 (0.00%)   | 0 / 25 (0.00%)   |
| occurrences (all)            | 0              | 0                | 0                |
| Haemorrhoids                 |                |                  |                  |
| subjects affected / exposed  | 1 / 6 (16.67%) | 0 / 44 (0.00%)   | 0 / 25 (0.00%)   |
| occurrences (all)            | 1              | 0                | 0                |
| Nausea                       |                |                  |                  |
| subjects affected / exposed  | 3 / 6 (50.00%) | 12 / 44 (27.27%) | 13 / 25 (52.00%) |
| occurrences (all)            | 4              | 14               | 22               |

|                                  |                |                |                 |
|----------------------------------|----------------|----------------|-----------------|
| Oral pain                        |                |                |                 |
| subjects affected / exposed      | 0 / 6 (0.00%)  | 1 / 44 (2.27%) | 0 / 25 (0.00%)  |
| occurrences (all)                | 0              | 1              | 0               |
| Stomatitis                       |                |                |                 |
| subjects affected / exposed      | 1 / 6 (16.67%) | 2 / 44 (4.55%) | 2 / 25 (8.00%)  |
| occurrences (all)                | 1              | 2              | 2               |
| Vomiting                         |                |                |                 |
| subjects affected / exposed      | 2 / 6 (33.33%) | 4 / 44 (9.09%) | 9 / 25 (36.00%) |
| occurrences (all)                | 2              | 5              | 19              |
| Abdominal tenderness             |                |                |                 |
| subjects affected / exposed      | 0 / 6 (0.00%)  | 0 / 44 (0.00%) | 0 / 25 (0.00%)  |
| occurrences (all)                | 0              | 0              | 0               |
| Aphthous ulcer                   |                |                |                 |
| subjects affected / exposed      | 0 / 6 (0.00%)  | 0 / 44 (0.00%) | 0 / 25 (0.00%)  |
| occurrences (all)                | 0              | 0              | 0               |
| Autoimmune colitis               |                |                |                 |
| subjects affected / exposed      | 0 / 6 (0.00%)  | 0 / 44 (0.00%) | 0 / 25 (0.00%)  |
| occurrences (all)                | 0              | 0              | 0               |
| Ascites                          |                |                |                 |
| subjects affected / exposed      | 1 / 6 (16.67%) | 0 / 44 (0.00%) | 0 / 25 (0.00%)  |
| occurrences (all)                | 2              | 0              | 0               |
| Chronic gastritis                |                |                |                 |
| subjects affected / exposed      | 0 / 6 (0.00%)  | 0 / 44 (0.00%) | 0 / 25 (0.00%)  |
| occurrences (all)                | 0              | 0              | 0               |
| Faecaloma                        |                |                |                 |
| subjects affected / exposed      | 0 / 6 (0.00%)  | 0 / 44 (0.00%) | 0 / 25 (0.00%)  |
| occurrences (all)                | 0              | 0              | 0               |
| Gastrooesophageal reflux disease |                |                |                 |
| subjects affected / exposed      | 0 / 6 (0.00%)  | 2 / 44 (4.55%) | 1 / 25 (4.00%)  |
| occurrences (all)                | 0              | 3              | 1               |
| Hepatobiliary disorders          |                |                |                 |
| Hepatic pain                     |                |                |                 |
| subjects affected / exposed      | 1 / 6 (16.67%) | 3 / 44 (6.82%) | 0 / 25 (0.00%)  |
| occurrences (all)                | 1              | 5              | 0               |
| Hypertransaminasaemia            |                |                |                 |



|  |                |                |                |
|--|----------------|----------------|----------------|
| subjects affected / exposed            | 0 / 6 (0.00%)  | 0 / 44 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all)                      | 0              | 0              | 0              |
| Bile duct obstruction                  |                |                |                |
| subjects affected / exposed            | 0 / 6 (0.00%)  | 0 / 44 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all)                      | 0              | 0              | 0              |
| Cholelithiasis                         |                |                |                |
| subjects affected / exposed            | 0 / 6 (0.00%)  | 0 / 44 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all)                      | 0              | 0              | 0              |
| Skin and subcutaneous tissue disorders |                |                |                |
| Alopecia                               |                |                |                |
| subjects affected / exposed            | 2 / 6 (33.33%) | 0 / 44 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all)                      | 2              | 0              | 0              |
| Actinic keratosis                      |                |                |                |
| subjects affected / exposed            | 0 / 6 (0.00%)  | 0 / 44 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all)                      | 0              | 0              | 0              |
| Dermatitis acneiform                   |                |                |                |
| subjects affected / exposed            | 0 / 6 (0.00%)  | 0 / 44 (0.00%) | 1 / 25 (4.00%) |
| occurrences (all)                      | 0              | 0              | 1              |
| Dry skin                               |                |                |                |
| subjects affected / exposed            | 0 / 6 (0.00%)  | 4 / 44 (9.09%) | 0 / 25 (0.00%) |
| occurrences (all)                      | 0              | 6              | 0              |
| Dermatitis exfoliative generalised     |                |                |                |
| subjects affected / exposed            | 0 / 6 (0.00%)  | 0 / 44 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all)                      | 0              | 0              | 0              |
| Hyperhidrosis                          |                |                |                |
| subjects affected / exposed            | 1 / 6 (16.67%) | 1 / 44 (2.27%) | 0 / 25 (0.00%) |
| occurrences (all)                      | 1              | 1              | 0              |
| Eczema nummular                        |                |                |                |
| subjects affected / exposed            | 0 / 6 (0.00%)  | 0 / 44 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all)                      | 0              | 0              | 0              |
| Lichenoid keratosis                    |                |                |                |
| subjects affected / exposed            | 0 / 6 (0.00%)  | 0 / 44 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all)                      | 0              | 0              | 0              |
| Livedo reticularis                     |                |                |                |
| subjects affected / exposed            | 0 / 6 (0.00%)  | 0 / 44 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all)                      | 0              | 0              | 0              |

|                             |                |                  |                 |
|-----------------------------|----------------|------------------|-----------------|
| Pruritus                    |                |                  |                 |
| subjects affected / exposed | 2 / 6 (33.33%) | 12 / 44 (27.27%) | 8 / 25 (32.00%) |
| occurrences (all)           | 2              | 17               | 8               |
| Rash                        |                |                  |                 |
| subjects affected / exposed | 1 / 6 (16.67%) | 11 / 44 (25.00%) | 6 / 25 (24.00%) |
| occurrences (all)           | 1              | 13               | 8               |
| Rash erythematous           |                |                  |                 |
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 44 (0.00%)   | 0 / 25 (0.00%)  |
| occurrences (all)           | 0              | 0                | 0               |
| Rash maculo-papular         |                |                  |                 |
| subjects affected / exposed | 0 / 6 (0.00%)  | 5 / 44 (11.36%)  | 4 / 25 (16.00%) |
| occurrences (all)           | 0              | 9                | 4               |
| Rash papular                |                |                  |                 |
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 44 (0.00%)   | 0 / 25 (0.00%)  |
| occurrences (all)           | 0              | 0                | 0               |
| Rash pruritic               |                |                  |                 |
| subjects affected / exposed | 0 / 6 (0.00%)  | 1 / 44 (2.27%)   | 3 / 25 (12.00%) |
| occurrences (all)           | 0              | 2                | 3               |
| Scab                        |                |                  |                 |
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 44 (0.00%)   | 0 / 25 (0.00%)  |
| occurrences (all)           | 0              | 0                | 0               |
| Skin hypopigmentation       |                |                  |                 |
| subjects affected / exposed | 0 / 6 (0.00%)  | 1 / 44 (2.27%)   | 1 / 25 (4.00%)  |
| occurrences (all)           | 0              | 1                | 1               |
| Vitiligo                    |                |                  |                 |
| subjects affected / exposed | 0 / 6 (0.00%)  | 6 / 44 (13.64%)  | 0 / 25 (0.00%)  |
| occurrences (all)           | 0              | 6                | 0               |
| Erythema                    |                |                  |                 |
| subjects affected / exposed | 0 / 6 (0.00%)  | 1 / 44 (2.27%)   | 0 / 25 (0.00%)  |
| occurrences (all)           | 0              | 1                | 0               |
| Night sweats                |                |                  |                 |
| subjects affected / exposed | 0 / 6 (0.00%)  | 1 / 44 (2.27%)   | 0 / 25 (0.00%)  |
| occurrences (all)           | 0              | 2                | 0               |
| Scar pain                   |                |                  |                 |
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 44 (0.00%)   | 0 / 25 (0.00%)  |
| occurrences (all)           | 0              | 0                | 0               |

|                             |                |                |                |
|-----------------------------|----------------|----------------|----------------|
| Skin ulcer                  |                |                |                |
| subjects affected / exposed | 0 / 6 (0.00%)  | 1 / 44 (2.27%) | 0 / 25 (0.00%) |
| occurrences (all)           | 0              | 1              | 0              |
| Facial wasting              |                |                |                |
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 44 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Renal and urinary disorders |                |                |                |
| Chromaturia                 |                |                |                |
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 44 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Acute kidney injury         |                |                |                |
| subjects affected / exposed | 1 / 6 (16.67%) | 1 / 44 (2.27%) | 1 / 25 (4.00%) |
| occurrences (all)           | 1              | 1              | 1              |
| Dysuria                     |                |                |                |
| subjects affected / exposed | 0 / 6 (0.00%)  | 2 / 44 (4.55%) | 1 / 25 (4.00%) |
| occurrences (all)           | 0              | 2              | 1              |
| Pollakiuria                 |                |                |                |
| subjects affected / exposed | 0 / 6 (0.00%)  | 1 / 44 (2.27%) | 0 / 25 (0.00%) |
| occurrences (all)           | 0              | 1              | 0              |
| Haematuria                  |                |                |                |
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 44 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Nocturia                    |                |                |                |
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 44 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Polyuria                    |                |                |                |
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 44 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Urinary hesitation          |                |                |                |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 44 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all)           | 1              | 0              | 0              |
| Urinary incontinence        |                |                |                |
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 44 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Endocrine disorders         |                |                |                |

|   |                |                  |                 |
|---|----------------|------------------|-----------------|
| Adrenal insufficiency                           |                |                  |                 |
| subjects affected / exposed                     | 1 / 6 (16.67%) | 0 / 44 (0.00%)   | 4 / 25 (16.00%) |
| occurrences (all)                               | 1              | 0                | 4               |
| Endocrine disorder                              |                |                  |                 |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 44 (0.00%)   | 0 / 25 (0.00%)  |
| occurrences (all)                               | 0              | 0                | 0               |
| Hyperthyroidism                                 |                |                  |                 |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 2 / 44 (4.55%)   | 4 / 25 (16.00%) |
| occurrences (all)                               | 0              | 2                | 4               |
| Hypophysitis                                    |                |                  |                 |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 44 (0.00%)   | 2 / 25 (8.00%)  |
| occurrences (all)                               | 0              | 0                | 2               |
| Hypothyroidism                                  |                |                  |                 |
| subjects affected / exposed                     | 2 / 6 (33.33%) | 5 / 44 (11.36%)  | 5 / 25 (20.00%) |
| occurrences (all)                               | 2              | 7                | 6               |
| Thyroiditis                                     |                |                  |                 |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 44 (0.00%)   | 0 / 25 (0.00%)  |
| occurrences (all)                               | 0              | 0                | 0               |
| Musculoskeletal and connective tissue disorders |                |                  |                 |
| Arthralgia                                      |                |                  |                 |
| subjects affected / exposed                     | 2 / 6 (33.33%) | 13 / 44 (29.55%) | 5 / 25 (20.00%) |
| occurrences (all)                               | 2              | 18               | 5               |
| Arthritis                                       |                |                  |                 |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 44 (0.00%)   | 1 / 25 (4.00%)  |
| occurrences (all)                               | 0              | 0                | 1               |
| Back pain                                       |                |                  |                 |
| subjects affected / exposed                     | 1 / 6 (16.67%) | 8 / 44 (18.18%)  | 1 / 25 (4.00%)  |
| occurrences (all)                               | 1              | 9                | 1               |
| Bone pain                                       |                |                  |                 |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 44 (0.00%)   | 1 / 25 (4.00%)  |
| occurrences (all)                               | 0              | 0                | 1               |
| Flank pain                                      |                |                  |                 |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 44 (0.00%)   | 0 / 25 (0.00%)  |
| occurrences (all)                               | 0              | 0                | 0               |
| Joint range of motion decreased                 |                |                  |                 |

|                             |                |                 |                 |
|-----------------------------|----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 44 (0.00%)  | 0 / 25 (0.00%)  |
| occurrences (all)           | 0              | 0               | 0               |
| Muscle spasms               |                |                 |                 |
| subjects affected / exposed | 0 / 6 (0.00%)  | 3 / 44 (6.82%)  | 0 / 25 (0.00%)  |
| occurrences (all)           | 0              | 3               | 0               |
| Musculoskeletal pain        |                |                 |                 |
| subjects affected / exposed | 0 / 6 (0.00%)  | 6 / 44 (13.64%) | 1 / 25 (4.00%)  |
| occurrences (all)           | 0              | 6               | 1               |
| Muscular weakness           |                |                 |                 |
| subjects affected / exposed | 1 / 6 (16.67%) | 3 / 44 (6.82%)  | 1 / 25 (4.00%)  |
| occurrences (all)           | 1              | 3               | 1               |
| Neck pain                   |                |                 |                 |
| subjects affected / exposed | 0 / 6 (0.00%)  | 5 / 44 (11.36%) | 2 / 25 (8.00%)  |
| occurrences (all)           | 0              | 5               | 2               |
| Myalgia                     |                |                 |                 |
| subjects affected / exposed | 1 / 6 (16.67%) | 7 / 44 (15.91%) | 3 / 25 (12.00%) |
| occurrences (all)           | 2              | 7               | 3               |
| Pain in extremity           |                |                 |                 |
| subjects affected / exposed | 0 / 6 (0.00%)  | 5 / 44 (11.36%) | 1 / 25 (4.00%)  |
| occurrences (all)           | 0              | 6               | 1               |
| Pain in jaw                 |                |                 |                 |
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 44 (0.00%)  | 1 / 25 (4.00%)  |
| occurrences (all)           | 0              | 0               | 1               |
| Musculoskeletal stiffness   |                |                 |                 |
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 44 (0.00%)  | 1 / 25 (4.00%)  |
| occurrences (all)           | 0              | 0               | 1               |
| Infections and infestations |                |                 |                 |
| Candida infection           |                |                 |                 |
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 44 (0.00%)  | 1 / 25 (4.00%)  |
| occurrences (all)           | 0              | 0               | 1               |
| Cellulitis                  |                |                 |                 |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 44 (0.00%)  | 1 / 25 (4.00%)  |
| occurrences (all)           | 1              | 0               | 1               |
| Conjunctivitis              |                |                 |                 |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 44 (0.00%)  | 2 / 25 (8.00%)  |
| occurrences (all)           | 1              | 0               | 3               |

|                                   |                |                |                |
|-----------------------------------|----------------|----------------|----------------|
| Influenza                         |                |                |                |
| subjects affected / exposed       | 0 / 6 (0.00%)  | 1 / 44 (2.27%) | 0 / 25 (0.00%) |
| occurrences (all)                 | 0              | 1              | 0              |
| Cytomegalovirus infection         |                |                |                |
| subjects affected / exposed       | 0 / 6 (0.00%)  | 0 / 44 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all)                 | 0              | 0              | 0              |
| Pneumonia                         |                |                |                |
| subjects affected / exposed       | 0 / 6 (0.00%)  | 0 / 44 (0.00%) | 1 / 25 (4.00%) |
| occurrences (all)                 | 0              | 0              | 1              |
| Nasopharyngitis                   |                |                |                |
| subjects affected / exposed       | 0 / 6 (0.00%)  | 0 / 44 (0.00%) | 1 / 25 (4.00%) |
| occurrences (all)                 | 0              | 0              | 1              |
| Rash pustular                     |                |                |                |
| subjects affected / exposed       | 0 / 6 (0.00%)  | 0 / 44 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all)                 | 0              | 0              | 0              |
| Respiratory tract infection       |                |                |                |
| subjects affected / exposed       | 0 / 6 (0.00%)  | 0 / 44 (0.00%) | 1 / 25 (4.00%) |
| occurrences (all)                 | 0              | 0              | 1              |
| Rhinitis                          |                |                |                |
| subjects affected / exposed       | 0 / 6 (0.00%)  | 2 / 44 (4.55%) | 0 / 25 (0.00%) |
| occurrences (all)                 | 0              | 2              | 0              |
| Sepsis                            |                |                |                |
| subjects affected / exposed       | 2 / 6 (33.33%) | 0 / 44 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all)                 | 2              | 0              | 0              |
| Sinusitis                         |                |                |                |
| subjects affected / exposed       | 1 / 6 (16.67%) | 3 / 44 (6.82%) | 1 / 25 (4.00%) |
| occurrences (all)                 | 1              | 3              | 1              |
| Skin infection                    |                |                |                |
| subjects affected / exposed       | 0 / 6 (0.00%)  | 1 / 44 (2.27%) | 1 / 25 (4.00%) |
| occurrences (all)                 | 0              | 2              | 1              |
| Upper respiratory tract infection |                |                |                |
| subjects affected / exposed       | 2 / 6 (33.33%) | 4 / 44 (9.09%) | 2 / 25 (8.00%) |
| occurrences (all)                 | 2              | 4              | 2              |
| Urinary tract infection           |                |                |                |
| subjects affected / exposed       | 2 / 6 (33.33%) | 3 / 44 (6.82%) | 0 / 25 (0.00%) |
| occurrences (all)                 | 2              | 3              | 0              |

|                                    |                |                  |                 |
|------------------------------------|----------------|------------------|-----------------|
| Fungal skin infection              |                |                  |                 |
| subjects affected / exposed        | 0 / 6 (0.00%)  | 0 / 44 (0.00%)   | 0 / 25 (0.00%)  |
| occurrences (all)                  | 0              | 0                | 0               |
| Hordeolum                          |                |                  |                 |
| subjects affected / exposed        | 0 / 6 (0.00%)  | 0 / 44 (0.00%)   | 0 / 25 (0.00%)  |
| occurrences (all)                  | 0              | 0                | 0               |
| Infected skin ulcer                |                |                  |                 |
| subjects affected / exposed        | 1 / 6 (16.67%) | 0 / 44 (0.00%)   | 0 / 25 (0.00%)  |
| occurrences (all)                  | 1              | 0                | 0               |
| Laryngitis                         |                |                  |                 |
| subjects affected / exposed        | 1 / 6 (16.67%) | 0 / 44 (0.00%)   | 0 / 25 (0.00%)  |
| occurrences (all)                  | 1              | 0                | 0               |
| Onychomycosis                      |                |                  |                 |
| subjects affected / exposed        | 0 / 6 (0.00%)  | 0 / 44 (0.00%)   | 0 / 25 (0.00%)  |
| occurrences (all)                  | 0              | 0                | 0               |
| Oral candidiasis                   |                |                  |                 |
| subjects affected / exposed        | 0 / 6 (0.00%)  | 0 / 44 (0.00%)   | 0 / 25 (0.00%)  |
| occurrences (all)                  | 0              | 0                | 0               |
| Oral herpes                        |                |                  |                 |
| subjects affected / exposed        | 0 / 6 (0.00%)  | 2 / 44 (4.55%)   | 0 / 25 (0.00%)  |
| occurrences (all)                  | 0              | 2                | 0               |
| Pyuria                             |                |                  |                 |
| subjects affected / exposed        | 0 / 6 (0.00%)  | 0 / 44 (0.00%)   | 0 / 25 (0.00%)  |
| occurrences (all)                  | 0              | 0                | 0               |
| Staphylococcal infection           |                |                  |                 |
| subjects affected / exposed        | 0 / 6 (0.00%)  | 0 / 44 (0.00%)   | 0 / 25 (0.00%)  |
| occurrences (all)                  | 0              | 0                | 0               |
| Herpes zoster                      |                |                  |                 |
| subjects affected / exposed        | 0 / 6 (0.00%)  | 0 / 44 (0.00%)   | 0 / 25 (0.00%)  |
| occurrences (all)                  | 0              | 0                | 0               |
| Metabolism and nutrition disorders |                |                  |                 |
| Decreased appetite                 |                |                  |                 |
| subjects affected / exposed        | 2 / 6 (33.33%) | 15 / 44 (34.09%) | 4 / 25 (16.00%) |
| occurrences (all)                  | 2              | 16               | 5               |
| Dehydration                        |                |                  |                 |

|                             |                |                |                |
|-----------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 3 / 6 (50.00%) | 0 / 44 (0.00%) | 2 / 25 (8.00%) |
| occurrences (all)           | 3              | 0              | 2              |
| Hypercalcaemia              |                |                |                |
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 44 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Hyperglycaemia              |                |                |                |
| subjects affected / exposed | 1 / 6 (16.67%) | 4 / 44 (9.09%) | 2 / 25 (8.00%) |
| occurrences (all)           | 1              | 7              | 2              |
| Hyperuricaemia              |                |                |                |
| subjects affected / exposed | 1 / 6 (16.67%) | 1 / 44 (2.27%) | 0 / 25 (0.00%) |
| occurrences (all)           | 1              | 1              | 0              |
| Hypoalbuminaemia            |                |                |                |
| subjects affected / exposed | 2 / 6 (33.33%) | 1 / 44 (2.27%) | 0 / 25 (0.00%) |
| occurrences (all)           | 2              | 1              | 0              |
| Hypoglycaemia               |                |                |                |
| subjects affected / exposed | 0 / 6 (0.00%)  | 1 / 44 (2.27%) | 0 / 25 (0.00%) |
| occurrences (all)           | 0              | 1              | 0              |
| Hypokalaemia                |                |                |                |
| subjects affected / exposed | 3 / 6 (50.00%) | 1 / 44 (2.27%) | 2 / 25 (8.00%) |
| occurrences (all)           | 4              | 1              | 3              |
| Hypomagnesaemia             |                |                |                |
| subjects affected / exposed | 1 / 6 (16.67%) | 1 / 44 (2.27%) | 2 / 25 (8.00%) |
| occurrences (all)           | 1              | 1              | 2              |
| Hyponatraemia               |                |                |                |
| subjects affected / exposed | 4 / 6 (66.67%) | 3 / 44 (6.82%) | 2 / 25 (8.00%) |
| occurrences (all)           | 4              | 3              | 3              |
| Hypophosphataemia           |                |                |                |
| subjects affected / exposed | 2 / 6 (33.33%) | 2 / 44 (4.55%) | 0 / 25 (0.00%) |
| occurrences (all)           | 3              | 3              | 0              |
| Lactic acidosis             |                |                |                |
| subjects affected / exposed | 2 / 6 (33.33%) | 0 / 44 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all)           | 2              | 0              | 0              |
| Malnutrition                |                |                |                |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 44 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all)           | 1              | 0              | 0              |
| Diabetes mellitus           |                |                |                |



|                             |                |                |                |
|-----------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 44 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all)           | 0              | 0              | 0              |
| Fluid retention             |                |                |                |
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 44 (0.00%) | 1 / 25 (4.00%) |
| occurrences (all)           | 0              | 0              | 1              |
| Hyperkalaemia               |                |                |                |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 44 (0.00%) | 1 / 25 (4.00%) |
| occurrences (all)           | 1              | 0              | 1              |
| Hypocalcaemia               |                |                |                |
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 44 (0.00%) | 1 / 25 (4.00%) |
| occurrences (all)           | 0              | 0              | 1              |
| Hypophagia                  |                |                |                |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 44 (0.00%) | 0 / 25 (0.00%) |
| occurrences (all)           | 1              | 0              | 0              |

| <b>Non-serious adverse events</b>                                   | N1 30M + I3 30M<br>BM | N3 30M non-BM    | I3 Monotherapy  |
|---|-----------------------|------------------|-----------------|
| Total subjects affected by non-serious adverse events               |                       |                  |                 |
| subjects affected / exposed   | 10 / 10 (100.00%)     | 10 / 11 (90.91%) | 1 / 1 (100.00%) |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                       |                  |                 |
| Malignant neoplasm progression                                      |                       |                  |                 |
| subjects affected / exposed   | 0 / 10 (0.00%)        | 0 / 11 (0.00%)   | 0 / 1 (0.00%)   |
| occurrences (all)   | 0                     | 0                | 0               |
| Tumour pain   |                       |                  |                 |
| subjects affected / exposed   | 0 / 10 (0.00%)        | 1 / 11 (9.09%)   | 0 / 1 (0.00%)   |
| occurrences (all)   | 0                     | 1                | 0               |
| Tumour embolism   |                       |                  |                 |
| subjects affected / exposed   | 0 / 10 (0.00%)        | 0 / 11 (0.00%)   | 0 / 1 (0.00%)   |
| occurrences (all)   | 0                     | 0                | 0               |
| Oncologic complication  |                       |                  |                 |
| subjects affected / exposed   | 0 / 10 (0.00%)        | 0 / 11 (0.00%)   | 0 / 1 (0.00%)   |
| occurrences (all)   | 0                     | 0                | 0               |
| Vascular disorders  |                       |                  |                 |
| Embolism  |                       |                  |                 |
| subjects affected / exposed   | 1 / 10 (10.00%)       | 0 / 11 (0.00%)   | 0 / 1 (0.00%)   |
| occurrences (all)   | 1                     | 0                | 0               |
| Flushing  |                       |                  |                 |

|  |                 |                 |                 |
|--|-----------------|-----------------|-----------------|
| subjects affected / exposed                          | 1 / 10 (10.00%) | 0 / 11 (0.00%)  | 0 / 1 (0.00%)   |
| occurrences (all)                                    | 1               | 0               | 0               |
| Hypertension   |                 |                 |                 |
| subjects affected / exposed                          | 1 / 10 (10.00%) | 0 / 11 (0.00%)  | 0 / 1 (0.00%)   |
| occurrences (all)                                    | 1               | 0               | 0               |
| Hypotension  |                 |                 |                 |
| subjects affected / exposed                          | 0 / 10 (0.00%)  | 0 / 11 (0.00%)  | 0 / 1 (0.00%)   |
| occurrences (all)                                    | 0               | 0               | 0               |
| Lymphoedema  |                 |                 |                 |
| subjects affected / exposed                          | 0 / 10 (0.00%)  | 0 / 11 (0.00%)  | 0 / 1 (0.00%)   |
| occurrences (all)                                    | 0               | 0               | 0               |
| Hot flush  |                 |                 |                 |
| subjects affected / exposed                          | 0 / 10 (0.00%)  | 0 / 11 (0.00%)  | 0 / 1 (0.00%)   |
| occurrences (all)                                    | 0               | 0               | 0               |
| Orthostatic hypotension                              |                 |                 |                 |
| subjects affected / exposed                          | 0 / 10 (0.00%)  | 0 / 11 (0.00%)  | 0 / 1 (0.00%)   |
| occurrences (all)                                    | 0               | 0               | 0               |
| General disorders and administration site conditions |                 |                 |                 |
| Asthenia   |                 |                 |                 |
| subjects affected / exposed                          | 1 / 10 (10.00%) | 0 / 11 (0.00%)  | 0 / 1 (0.00%)   |
| occurrences (all)                                    | 1               | 0               | 0               |
| Chest pain   |                 |                 |                 |
| subjects affected / exposed                          | 0 / 10 (0.00%)  | 0 / 11 (0.00%)  | 0 / 1 (0.00%)   |
| occurrences (all)                                    | 0               | 0               | 0               |
| Chills   |                 |                 |                 |
| subjects affected / exposed                          | 2 / 10 (20.00%) | 0 / 11 (0.00%)  | 0 / 1 (0.00%)   |
| occurrences (all)                                    | 2               | 0               | 0               |
| Fatigue  |                 |                 |                 |
| subjects affected / exposed                          | 6 / 10 (60.00%) | 5 / 11 (45.45%) | 1 / 1 (100.00%) |
| occurrences (all)                                    | 8               | 5               | 1               |
| Hernia pain  |                 |                 |                 |
| subjects affected / exposed                          | 0 / 10 (0.00%)  | 0 / 11 (0.00%)  | 0 / 1 (0.00%)   |
| occurrences (all)                                    | 0               | 0               | 0               |
| Influenza like illness                               |                 |                 |                 |

|                             |                 |                 |               |
|-----------------------------|-----------------|-----------------|---------------|
| subjects affected / exposed | 3 / 10 (30.00%) | 1 / 11 (9.09%)  | 0 / 1 (0.00%) |
| occurrences (all)           | 4               | 1               | 0             |
| Localised oedema            |                 |                 |               |
| subjects affected / exposed | 0 / 10 (0.00%)  | 1 / 11 (9.09%)  | 0 / 1 (0.00%) |
| occurrences (all)           | 0               | 1               | 0             |
| Malaise                     |                 |                 |               |
| subjects affected / exposed | 1 / 10 (10.00%) | 0 / 11 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)           | 1               | 0               | 0             |
| Mucosal inflammation        |                 |                 |               |
| subjects affected / exposed | 0 / 10 (0.00%)  | 0 / 11 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)           | 0               | 0               | 0             |
| Non-cardiac chest pain      |                 |                 |               |
| subjects affected / exposed | 0 / 10 (0.00%)  | 0 / 11 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)           | 0               | 0               | 0             |
| Oedema peripheral           |                 |                 |               |
| subjects affected / exposed | 4 / 10 (40.00%) | 0 / 11 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)           | 4               | 0               | 0             |
| Pain                        |                 |                 |               |
| subjects affected / exposed | 1 / 10 (10.00%) | 0 / 11 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)           | 1               | 0               | 0             |
| Peripheral swelling         |                 |                 |               |
| subjects affected / exposed | 1 / 10 (10.00%) | 0 / 11 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)           | 1               | 0               | 0             |
| Pyrexia                     |                 |                 |               |
| subjects affected / exposed | 5 / 10 (50.00%) | 3 / 11 (27.27%) | 0 / 1 (0.00%) |
| occurrences (all)           | 8               | 3               | 0             |
| Temperature intolerance     |                 |                 |               |
| subjects affected / exposed | 1 / 10 (10.00%) | 0 / 11 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)           | 1               | 0               | 0             |
| Decreased activity          |                 |                 |               |
| subjects affected / exposed | 0 / 10 (0.00%)  | 0 / 11 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)           | 0               | 0               | 0             |
| Feeling cold                |                 |                 |               |
| subjects affected / exposed | 0 / 10 (0.00%)  | 0 / 11 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)           | 0               | 0               | 0             |
| Gait disturbance            |                 |                 |               |

|   |                |                |               |
|---|----------------|----------------|---------------|
| subjects affected / exposed                     | 0 / 10 (0.00%) | 0 / 11 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)                               | 0              | 0              | 0             |
| Feeling of body temperature change              |                |                |               |
| subjects affected / exposed                     | 0 / 10 (0.00%) | 0 / 11 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)                               | 0              | 0              | 0             |
| Inflammation                                    |                |                |               |
| subjects affected / exposed                     | 0 / 10 (0.00%) | 0 / 11 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)                               | 0              | 0              | 0             |
| Physical deconditioning                         |                |                |               |
| subjects affected / exposed                     | 0 / 10 (0.00%) | 0 / 11 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)                               | 0              | 0              | 0             |
| Axillary pain                                   |                |                |               |
| subjects affected / exposed                     | 0 / 10 (0.00%) | 0 / 11 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)                               | 0              | 0              | 0             |
| Immune system disorders                         |                |                |               |
| Drug hypersensitivity                           |                |                |               |
| subjects affected / exposed                     | 0 / 10 (0.00%) | 0 / 11 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)                               | 0              | 0              | 0             |
| Hypersensitivity                                |                |                |               |
| subjects affected / exposed                     | 0 / 10 (0.00%) | 1 / 11 (9.09%) | 0 / 1 (0.00%) |
| occurrences (all)                               | 0              | 1              | 0             |
| Reproductive system and breast disorders        |                |                |               |
| Nipple pain                                     |                |                |               |
| subjects affected / exposed                     | 0 / 10 (0.00%) | 0 / 11 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)                               | 0              | 0              | 0             |
| Spermatic cord haemorrhage                      |                |                |               |
| subjects affected / exposed                     | 0 / 10 (0.00%) | 1 / 11 (9.09%) | 0 / 1 (0.00%) |
| occurrences (all)                               | 0              | 1              | 0             |
| Genital rash                                    |                |                |               |
| subjects affected / exposed                     | 0 / 10 (0.00%) | 0 / 11 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)                               | 0              | 0              | 0             |
| Scrotal swelling                                |                |                |               |
| subjects affected / exposed                     | 0 / 10 (0.00%) | 0 / 11 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)                               | 0              | 0              | 0             |
| Respiratory, thoracic and mediastinal disorders |                |                |               |

|                             |                 |                |               |
|-----------------------------|-----------------|----------------|---------------|
| Bronchial obstruction       |                 |                |               |
| subjects affected / exposed | 0 / 10 (0.00%)  | 0 / 11 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 0               | 0              | 0             |
| Cough                       |                 |                |               |
| subjects affected / exposed | 3 / 10 (30.00%) | 1 / 11 (9.09%) | 0 / 1 (0.00%) |
| occurrences (all)           | 3               | 1              | 0             |
| Dyspnoea                    |                 |                |               |
| subjects affected / exposed | 2 / 10 (20.00%) | 1 / 11 (9.09%) | 0 / 1 (0.00%) |
| occurrences (all)           | 3               | 1              | 0             |
| Hypoxia                     |                 |                |               |
| subjects affected / exposed | 0 / 10 (0.00%)  | 0 / 11 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 0               | 0              | 0             |
| Oropharyngeal pain          |                 |                |               |
| subjects affected / exposed | 1 / 10 (10.00%) | 0 / 11 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 1               | 0              | 0             |
| Nasal congestion            |                 |                |               |
| subjects affected / exposed | 0 / 10 (0.00%)  | 0 / 11 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 0               | 0              | 0             |
| Pleural effusion            |                 |                |               |
| subjects affected / exposed | 0 / 10 (0.00%)  | 0 / 11 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 0               | 0              | 0             |
| Pneumonitis                 |                 |                |               |
| subjects affected / exposed | 0 / 10 (0.00%)  | 1 / 11 (9.09%) | 0 / 1 (0.00%) |
| occurrences (all)           | 0               | 1              | 0             |
| Productive cough            |                 |                |               |
| subjects affected / exposed | 1 / 10 (10.00%) | 0 / 11 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 1               | 0              | 0             |
| Rhinitis allergic           |                 |                |               |
| subjects affected / exposed | 0 / 10 (0.00%)  | 1 / 11 (9.09%) | 0 / 1 (0.00%) |
| occurrences (all)           | 0               | 1              | 0             |
| Rhinorrhoea                 |                 |                |               |
| subjects affected / exposed | 0 / 10 (0.00%)  | 1 / 11 (9.09%) | 0 / 1 (0.00%) |
| occurrences (all)           | 0               | 1              | 0             |
| Upper-airway cough syndrome |                 |                |               |
| subjects affected / exposed | 0 / 10 (0.00%)  | 0 / 11 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 0               | 0              | 0             |

|                              |                |                |                 |
|------------------------------|----------------|----------------|-----------------|
| Dysphonia                    |                |                |                 |
| subjects affected / exposed  | 0 / 10 (0.00%) | 0 / 11 (0.00%) | 0 / 1 (0.00%)   |
| occurrences (all)            | 0              | 0              | 0               |
| Dyspnoea exertional          |                |                |                 |
| subjects affected / exposed  | 0 / 10 (0.00%) | 0 / 11 (0.00%) | 0 / 1 (0.00%)   |
| occurrences (all)            | 0              | 0              | 0               |
| Epistaxis                    |                |                |                 |
| subjects affected / exposed  | 0 / 10 (0.00%) | 0 / 11 (0.00%) | 0 / 1 (0.00%)   |
| occurrences (all)            | 0              | 0              | 0               |
| Haemoptysis                  |                |                |                 |
| subjects affected / exposed  | 0 / 10 (0.00%) | 0 / 11 (0.00%) | 0 / 1 (0.00%)   |
| occurrences (all)            | 0              | 0              | 0               |
| Hiccups                      |                |                |                 |
| subjects affected / exposed  | 0 / 10 (0.00%) | 0 / 11 (0.00%) | 0 / 1 (0.00%)   |
| occurrences (all)            | 0              | 0              | 0               |
| Pulmonary embolism           |                |                |                 |
| subjects affected / exposed  | 0 / 10 (0.00%) | 0 / 11 (0.00%) | 0 / 1 (0.00%)   |
| occurrences (all)            | 0              | 0              | 0               |
| Respiratory failure          |                |                |                 |
| subjects affected / exposed  | 0 / 10 (0.00%) | 0 / 11 (0.00%) | 0 / 1 (0.00%)   |
| occurrences (all)            | 0              | 0              | 0               |
| Respiratory tract congestion |                |                |                 |
| subjects affected / exposed  | 0 / 10 (0.00%) | 0 / 11 (0.00%) | 0 / 1 (0.00%)   |
| occurrences (all)            | 0              | 0              | 0               |
| Psychiatric disorders        |                |                |                 |
| Confusional state            |                |                |                 |
| subjects affected / exposed  | 0 / 10 (0.00%) | 0 / 11 (0.00%) | 0 / 1 (0.00%)   |
| occurrences (all)            | 0              | 0              | 0               |
| Anxiety                      |                |                |                 |
| subjects affected / exposed  | 0 / 10 (0.00%) | 0 / 11 (0.00%) | 1 / 1 (100.00%) |
| occurrences (all)            | 0              | 0              | 1               |
| Depression                   |                |                |                 |
| subjects affected / exposed  | 0 / 10 (0.00%) | 0 / 11 (0.00%) | 0 / 1 (0.00%)   |
| occurrences (all)            | 0              | 0              | 0               |
| Insomnia                     |                |                |                 |

|   |                 |                |               |
|---|-----------------|----------------|---------------|
| subjects affected / exposed                     | 3 / 10 (30.00%) | 1 / 11 (9.09%) | 0 / 1 (0.00%) |
| occurrences (all)                               | 3               | 1              | 0             |
| Sleep disorder                                  |                 |                |               |
| subjects affected / exposed                     | 1 / 10 (10.00%) | 0 / 11 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)                               | 1               | 0              | 0             |
| Depressed mood                                  |                 |                |               |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 0 / 11 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)                               | 0               | 0              | 0             |
| Disorientation                                  |                 |                |               |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 0 / 11 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)                               | 0               | 0              | 0             |
| Irritability                                    |                 |                |               |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 0 / 11 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)                               | 0               | 0              | 0             |
| Hallucination                                   |                 |                |               |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 0 / 11 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)                               | 0               | 0              | 0             |
| Mental status changes                           |                 |                |               |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 0 / 11 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)                               | 0               | 0              | 0             |
| Investigations                                  |                 |                |               |
| Activated partial thromboplastin time prolonged |                 |                |               |
| subjects affected / exposed                     | 1 / 10 (10.00%) | 0 / 11 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)                               | 1               | 0              | 0             |
| Alanine aminotransferase increased              |                 |                |               |
| subjects affected / exposed                     | 2 / 10 (20.00%) | 0 / 11 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)                               | 6               | 0              | 0             |
| Amylase increased                               |                 |                |               |
| subjects affected / exposed                     | 3 / 10 (30.00%) | 0 / 11 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)                               | 7               | 0              | 0             |
| Aspartate aminotransferase increased            |                 |                |               |
| subjects affected / exposed                     | 1 / 10 (10.00%) | 0 / 11 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)                               | 1               | 0              | 0             |
| Blood alkaline phosphatase increased            |                 |                |               |

|   |                 |                |                 |
|---|-----------------|----------------|-----------------|
| subjects affected / exposed                 | 0 / 10 (0.00%)  | 0 / 11 (0.00%) | 1 / 1 (100.00%) |
| occurrences (all)                           | 0               | 0              | 1               |
| Blood bilirubin increased                   |                 |                |                 |
| subjects affected / exposed                 | 1 / 10 (10.00%) | 1 / 11 (9.09%) | 0 / 1 (0.00%)   |
| occurrences (all)                           | 2               | 1              | 0               |
| Blood creatinine increased                  |                 |                |                 |
| subjects affected / exposed                 | 0 / 10 (0.00%)  | 0 / 11 (0.00%) | 0 / 1 (0.00%)   |
| occurrences (all)                           | 0               | 0              | 0               |
| Blood thyroid stimulating hormone decreased |                 |                |                 |
| subjects affected / exposed                 | 0 / 10 (0.00%)  | 0 / 11 (0.00%) | 0 / 1 (0.00%)   |
| occurrences (all)                           | 0               | 0              | 0               |
| Blood thyroid stimulating hormone increased |                 |                |                 |
| subjects affected / exposed                 | 0 / 10 (0.00%)  | 0 / 11 (0.00%) | 0 / 1 (0.00%)   |
| occurrences (all)                           | 0               | 0              | 0               |
| Cortisol increased                          |                 |                |                 |
| subjects affected / exposed                 | 1 / 10 (10.00%) | 0 / 11 (0.00%) | 0 / 1 (0.00%)   |
| occurrences (all)                           | 1               | 0              | 0               |
| Hepatic enzyme increased                    |                 |                |                 |
| subjects affected / exposed                 | 1 / 10 (10.00%) | 0 / 11 (0.00%) | 0 / 1 (0.00%)   |
| occurrences (all)                           | 1               | 0              | 0               |
| International normalised ratio increased    |                 |                |                 |
| subjects affected / exposed                 | 1 / 10 (10.00%) | 0 / 11 (0.00%) | 0 / 1 (0.00%)   |
| occurrences (all)                           | 1               | 0              | 0               |
| Lipase increased                            |                 |                |                 |
| subjects affected / exposed                 | 3 / 10 (30.00%) | 0 / 11 (0.00%) | 0 / 1 (0.00%)   |
| occurrences (all)                           | 11              | 0              | 0               |
| Lymphocyte count decreased                  |                 |                |                 |
| subjects affected / exposed                 | 0 / 10 (0.00%)  | 1 / 11 (9.09%) | 1 / 1 (100.00%) |
| occurrences (all)                           | 0               | 1              | 1               |
| Platelet count decreased                    |                 |                |                 |
| subjects affected / exposed                 | 0 / 10 (0.00%)  | 0 / 11 (0.00%) | 0 / 1 (0.00%)   |
| occurrences (all)                           | 0               | 0              | 0               |
| Norovirus test positive                     |                 |                |                 |



|  |                 |                |                 |
|--|-----------------|----------------|-----------------|
| subjects affected / exposed                    | 1 / 10 (10.00%) | 0 / 11 (0.00%) | 0 / 1 (0.00%)   |
| occurrences (all)                              | 1               | 0              | 0               |
| Transaminases increased                        |                 |                |                 |
| subjects affected / exposed                    | 0 / 10 (0.00%)  | 0 / 11 (0.00%) | 0 / 1 (0.00%)   |
| occurrences (all)                              | 0               | 0              | 0               |
| Weight decreased                               |                 |                |                 |
| subjects affected / exposed                    | 0 / 10 (0.00%)  | 0 / 11 (0.00%) | 1 / 1 (100.00%) |
| occurrences (all)                              | 0               | 0              | 1               |
| Weight increased                               |                 |                |                 |
| subjects affected / exposed                    | 2 / 10 (20.00%) | 0 / 11 (0.00%) | 0 / 1 (0.00%)   |
| occurrences (all)                              | 3               | 0              | 0               |
| Blood urea increased                           |                 |                |                 |
| subjects affected / exposed                    | 0 / 10 (0.00%)  | 0 / 11 (0.00%) | 0 / 1 (0.00%)   |
| occurrences (all)                              | 0               | 0              | 0               |
| Heart rate increased                           |                 |                |                 |
| subjects affected / exposed                    | 0 / 10 (0.00%)  | 0 / 11 (0.00%) | 0 / 1 (0.00%)   |
| occurrences (all)                              | 0               | 0              | 0               |
| Injury, poisoning and procedural complications |                 |                |                 |
| Contusion                                      |                 |                |                 |
| subjects affected / exposed                    | 0 / 10 (0.00%)  | 0 / 11 (0.00%) | 0 / 1 (0.00%)   |
| occurrences (all)                              | 0               | 0              | 0               |
| Infusion related reaction                      |                 |                |                 |
| subjects affected / exposed                    | 0 / 10 (0.00%)  | 0 / 11 (0.00%) | 0 / 1 (0.00%)   |
| occurrences (all)                              | 0               | 0              | 0               |
| Limb injury                                    |                 |                |                 |
| subjects affected / exposed                    | 0 / 10 (0.00%)  | 0 / 11 (0.00%) | 0 / 1 (0.00%)   |
| occurrences (all)                              | 0               | 0              | 0               |
| Procedural pain                                |                 |                |                 |
| subjects affected / exposed                    | 0 / 10 (0.00%)  | 0 / 11 (0.00%) | 0 / 1 (0.00%)   |
| occurrences (all)                              | 0               | 0              | 0               |
| Bone fissure                                   |                 |                |                 |
| subjects affected / exposed                    | 0 / 10 (0.00%)  | 0 / 11 (0.00%) | 0 / 1 (0.00%)   |
| occurrences (all)                              | 0               | 0              | 0               |
| Radiation pneumonitis                          |                 |                |                 |

|   |                      |                     |                    |
|---|----------------------|---------------------|--------------------|
| subjects affected / exposed<br>occurrences (all)  | 0 / 10 (0.00%)<br>0  | 0 / 11 (0.00%)<br>0 | 0 / 1 (0.00%)<br>0 |
| Fall<br>subjects affected / exposed<br>occurrences (all)                                  | 0 / 10 (0.00%)<br>0  | 0 / 11 (0.00%)<br>0 | 0 / 1 (0.00%)<br>0 |
| Cardiac disorders   |                      |                     |                    |
| Acute coronary syndrome<br>subjects affected / exposed<br>occurrences (all)               | 1 / 10 (10.00%)<br>1 | 0 / 11 (0.00%)<br>0 | 0 / 1 (0.00%)<br>0 |
| Angina pectoris<br>subjects affected / exposed<br>occurrences (all)                       | 0 / 10 (0.00%)<br>0  | 0 / 11 (0.00%)<br>0 | 0 / 1 (0.00%)<br>0 |
| Palpitations<br>subjects affected / exposed<br>occurrences (all)                          | 0 / 10 (0.00%)<br>0  | 0 / 11 (0.00%)<br>0 | 0 / 1 (0.00%)<br>0 |
| Tachycardia<br>subjects affected / exposed<br>occurrences (all)                           | 0 / 10 (0.00%)<br>0  | 0 / 11 (0.00%)<br>0 | 0 / 1 (0.00%)<br>0 |
| Cardiac failure congestive<br>subjects affected / exposed<br>occurrences (all)            | 0 / 10 (0.00%)<br>0  | 0 / 11 (0.00%)<br>0 | 0 / 1 (0.00%)<br>0 |
| Atrioventricular block second degree<br>subjects affected / exposed<br>occurrences (all)  | 0 / 10 (0.00%)<br>0  | 0 / 11 (0.00%)<br>0 | 0 / 1 (0.00%)<br>0 |
| Nervous system disorders  |                      |                     |                    |
| Autonomic nervous system<br>imbalance<br>subjects affected / exposed<br>occurrences (all) | 1 / 10 (10.00%)<br>1 | 0 / 11 (0.00%)<br>0 | 0 / 1 (0.00%)<br>0 |
| Cerebrovascular accident<br>subjects affected / exposed<br>occurrences (all)              | 1 / 10 (10.00%)<br>1 | 0 / 11 (0.00%)<br>0 | 0 / 1 (0.00%)<br>0 |
| Disturbance in attention<br>subjects affected / exposed<br>occurrences (all)              | 0 / 10 (0.00%)<br>0  | 0 / 11 (0.00%)<br>0 | 0 / 1 (0.00%)<br>0 |
| Dizziness   |                      |                     |                    |

|                             |                 |                 |               |
|-----------------------------|-----------------|-----------------|---------------|
| subjects affected / exposed | 2 / 10 (20.00%) | 3 / 11 (27.27%) | 0 / 1 (0.00%) |
| occurrences (all)           | 2               | 3               | 0             |
| Dysaesthesia                |                 |                 |               |
| subjects affected / exposed | 0 / 10 (0.00%)  | 0 / 11 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)           | 0               | 0               | 0             |
| Dysarthria                  |                 |                 |               |
| subjects affected / exposed | 1 / 10 (10.00%) | 0 / 11 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)           | 1               | 0               | 0             |
| Dysgeusia                   |                 |                 |               |
| subjects affected / exposed | 0 / 10 (0.00%)  | 0 / 11 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)           | 0               | 0               | 0             |
| Headache                    |                 |                 |               |
| subjects affected / exposed | 5 / 10 (50.00%) | 0 / 11 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)           | 6               | 0               | 0             |
| Hemiparesis                 |                 |                 |               |
| subjects affected / exposed | 0 / 10 (0.00%)  | 0 / 11 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)           | 0               | 0               | 0             |
| Lethargy                    |                 |                 |               |
| subjects affected / exposed | 0 / 10 (0.00%)  | 0 / 11 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)           | 0               | 0               | 0             |
| Neuropathy peripheral       |                 |                 |               |
| subjects affected / exposed | 1 / 10 (10.00%) | 0 / 11 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)           | 1               | 0               | 0             |
| Paraesthesia                |                 |                 |               |
| subjects affected / exposed | 0 / 10 (0.00%)  | 0 / 11 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)           | 0               | 0               | 0             |
| Presyncope                  |                 |                 |               |
| subjects affected / exposed | 1 / 10 (10.00%) | 0 / 11 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)           | 1               | 0               | 0             |
| Restless legs syndrome      |                 |                 |               |
| subjects affected / exposed | 1 / 10 (10.00%) | 0 / 11 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)           | 1               | 0               | 0             |
| Seizure                     |                 |                 |               |
| subjects affected / exposed | 1 / 10 (10.00%) | 0 / 11 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)           | 1               | 0               | 0             |
| Aphasia                     |                 |                 |               |

|                             |                |                |               |
|-----------------------------|----------------|----------------|---------------|
| subjects affected / exposed | 0 / 10 (0.00%) | 0 / 11 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 0              | 0              | 0             |
| Amnesia                     |                |                |               |
| subjects affected / exposed | 0 / 10 (0.00%) | 0 / 11 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 0              | 0              | 0             |
| Fine motor delay            |                |                |               |
| subjects affected / exposed | 0 / 10 (0.00%) | 0 / 11 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 0              | 0              | 0             |
| Encephalopathy              |                |                |               |
| subjects affected / exposed | 0 / 10 (0.00%) | 0 / 11 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 0              | 0              | 0             |
| Hypersomnia                 |                |                |               |
| subjects affected / exposed | 0 / 10 (0.00%) | 0 / 11 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 0              | 0              | 0             |
| Hypoaesthesia               |                |                |               |
| subjects affected / exposed | 0 / 10 (0.00%) | 0 / 11 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 0              | 0              | 0             |
| Mental impairment           |                |                |               |
| subjects affected / exposed | 0 / 10 (0.00%) | 0 / 11 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 0              | 0              | 0             |
| Muscle spasticity           |                |                |               |
| subjects affected / exposed | 0 / 10 (0.00%) | 0 / 11 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 0              | 0              | 0             |
| Neurotoxicity               |                |                |               |
| subjects affected / exposed | 0 / 10 (0.00%) | 0 / 11 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 0              | 0              | 0             |
| Somnolence                  |                |                |               |
| subjects affected / exposed | 0 / 10 (0.00%) | 0 / 11 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 0              | 0              | 0             |
| Syncope                     |                |                |               |
| subjects affected / exposed | 0 / 10 (0.00%) | 0 / 11 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 0              | 0              | 0             |
| Spinal cord compression     |                |                |               |
| subjects affected / exposed | 0 / 10 (0.00%) | 0 / 11 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 0              | 0              | 0             |
| Tremor                      |                |                |               |

|  |                      |                     |                      |
|--|----------------------|---------------------|----------------------|
| subjects affected / exposed<br>occurrences (all)                       | 0 / 10 (0.00%)<br>0  | 0 / 11 (0.00%)<br>0 | 0 / 1 (0.00%)<br>0   |
| Balance disorder<br>subjects affected / exposed<br>occurrences (all)   | 0 / 10 (0.00%)<br>0  | 0 / 11 (0.00%)<br>0 | 0 / 1 (0.00%)<br>0   |
| Blood and lymphatic system disorders                                   |                      |                     |                      |
| Anaemia<br>subjects affected / exposed<br>occurrences (all)            | 2 / 10 (20.00%)<br>4 | 0 / 11 (0.00%)<br>0 | 1 / 1 (100.00%)<br>1 |
| Haemolytic anaemia<br>subjects affected / exposed<br>occurrences (all) | 1 / 10 (10.00%)<br>1 | 0 / 11 (0.00%)<br>0 | 0 / 1 (0.00%)<br>0   |
| Thrombocytopenia<br>subjects affected / exposed<br>occurrences (all)   | 1 / 10 (10.00%)<br>1 | 0 / 11 (0.00%)<br>0 | 0 / 1 (0.00%)<br>0   |
| Coagulopathy<br>subjects affected / exposed<br>occurrences (all)       | 0 / 10 (0.00%)<br>0  | 0 / 11 (0.00%)<br>0 | 0 / 1 (0.00%)<br>0   |
| Lymphadenopathy<br>subjects affected / exposed<br>occurrences (all)    | 0 / 10 (0.00%)<br>0  | 0 / 11 (0.00%)<br>0 | 0 / 1 (0.00%)<br>0   |
| Microcytic anaemia<br>subjects affected / exposed<br>occurrences (all) | 0 / 10 (0.00%)<br>0  | 0 / 11 (0.00%)<br>0 | 0 / 1 (0.00%)<br>0   |
| Ear and labyrinth disorders  |                      |                     |                      |
| Hypoacusis<br>subjects affected / exposed<br>occurrences (all)         | 2 / 10 (20.00%)<br>2 | 0 / 11 (0.00%)<br>0 | 0 / 1 (0.00%)<br>0   |
| Cerumen impaction<br>subjects affected / exposed<br>occurrences (all)  | 0 / 10 (0.00%)<br>0  | 0 / 11 (0.00%)<br>0 | 0 / 1 (0.00%)<br>0   |
| Eye disorders  |                      |                     |                      |
| Dry eye<br>subjects affected / exposed<br>occurrences (all)            | 2 / 10 (20.00%)<br>2 | 0 / 11 (0.00%)<br>0 | 0 / 1 (0.00%)<br>0   |
| Eye disorder   |                      |                     |                      |

|                             |                 |                |               |
|-----------------------------|-----------------|----------------|---------------|
| subjects affected / exposed | 1 / 10 (10.00%) | 0 / 11 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 1               | 0              | 0             |
| Eye pain                    |                 |                |               |
| subjects affected / exposed | 0 / 10 (0.00%)  | 0 / 11 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 0               | 0              | 0             |
| Uveitis                     |                 |                |               |
| subjects affected / exposed | 1 / 10 (10.00%) | 0 / 11 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 1               | 0              | 0             |
| Vision blurred              |                 |                |               |
| subjects affected / exposed | 0 / 10 (0.00%)  | 0 / 11 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 0               | 0              | 0             |
| Visual impairment           |                 |                |               |
| subjects affected / exposed | 0 / 10 (0.00%)  | 0 / 11 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 0               | 0              | 0             |
| Eye pruritus                |                 |                |               |
| subjects affected / exposed | 0 / 10 (0.00%)  | 0 / 11 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 0               | 0              | 0             |
| Eye swelling                |                 |                |               |
| subjects affected / exposed | 0 / 10 (0.00%)  | 0 / 11 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 0               | 0              | 0             |
| Iridocyclitis               |                 |                |               |
| subjects affected / exposed | 0 / 10 (0.00%)  | 0 / 11 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 0               | 0              | 0             |
| Lacrimation increased       |                 |                |               |
| subjects affected / exposed | 0 / 10 (0.00%)  | 0 / 11 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 0               | 0              | 0             |
| Ocular hyperaemia           |                 |                |               |
| subjects affected / exposed | 0 / 10 (0.00%)  | 0 / 11 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 0               | 0              | 0             |
| Conjunctival oedema         |                 |                |               |
| subjects affected / exposed | 0 / 10 (0.00%)  | 0 / 11 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 0               | 0              | 0             |
| Gastrointestinal disorders  |                 |                |               |
| Abdominal discomfort        |                 |                |               |
| subjects affected / exposed | 1 / 10 (10.00%) | 0 / 11 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 1               | 0              | 0             |

|                             |                 |                 |                 |
|-----------------------------|-----------------|-----------------|-----------------|
| Abdominal distension        |                 |                 |                 |
| subjects affected / exposed | 0 / 10 (0.00%)  | 0 / 11 (0.00%)  | 0 / 1 (0.00%)   |
| occurrences (all)           | 0               | 0               | 0               |
| Abdominal pain              |                 |                 |                 |
| subjects affected / exposed | 0 / 10 (0.00%)  | 3 / 11 (27.27%) | 1 / 1 (100.00%) |
| occurrences (all)           | 0               | 3               | 1               |
| Abdominal pain upper        |                 |                 |                 |
| subjects affected / exposed | 2 / 10 (20.00%) | 0 / 11 (0.00%)  | 0 / 1 (0.00%)   |
| occurrences (all)           | 2               | 0               | 0               |
| Anal pruritus               |                 |                 |                 |
| subjects affected / exposed | 0 / 10 (0.00%)  | 0 / 11 (0.00%)  | 0 / 1 (0.00%)   |
| occurrences (all)           | 0               | 0               | 0               |
| Colitis                     |                 |                 |                 |
| subjects affected / exposed | 1 / 10 (10.00%) | 0 / 11 (0.00%)  | 0 / 1 (0.00%)   |
| occurrences (all)           | 1               | 0               | 0               |
| Constipation                |                 |                 |                 |
| subjects affected / exposed | 1 / 10 (10.00%) | 1 / 11 (9.09%)  | 0 / 1 (0.00%)   |
| occurrences (all)           | 2               | 1               | 0               |
| Diarrhoea                   |                 |                 |                 |
| subjects affected / exposed | 6 / 10 (60.00%) | 4 / 11 (36.36%) | 0 / 1 (0.00%)   |
| occurrences (all)           | 8               | 4               | 0               |
| Dry mouth                   |                 |                 |                 |
| subjects affected / exposed | 0 / 10 (0.00%)  | 1 / 11 (9.09%)  | 0 / 1 (0.00%)   |
| occurrences (all)           | 0               | 2               | 0               |
| Dyspepsia                   |                 |                 |                 |
| subjects affected / exposed | 1 / 10 (10.00%) | 0 / 11 (0.00%)  | 0 / 1 (0.00%)   |
| occurrences (all)           | 1               | 0               | 0               |
| Dysphagia                   |                 |                 |                 |
| subjects affected / exposed | 0 / 10 (0.00%)  | 1 / 11 (9.09%)  | 0 / 1 (0.00%)   |
| occurrences (all)           | 0               | 1               | 0               |
| Gastritis                   |                 |                 |                 |
| subjects affected / exposed | 0 / 10 (0.00%)  | 1 / 11 (9.09%)  | 0 / 1 (0.00%)   |
| occurrences (all)           | 0               | 1               | 0               |
| Flatulence                  |                 |                 |                 |
| subjects affected / exposed | 0 / 10 (0.00%)  | 0 / 11 (0.00%)  | 0 / 1 (0.00%)   |
| occurrences (all)           | 0               | 0               | 0               |

|  |                      |                      |                    |
|--|----------------------|----------------------|--------------------|
| Gastrointestinal haemorrhage<br>subjects affected / exposed<br>occurrences (all) | 0 / 10 (0.00%)<br>0  | 0 / 11 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0 |
| Haemorrhoids<br>subjects affected / exposed<br>occurrences (all)                 | 0 / 10 (0.00%)<br>0  | 0 / 11 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0 |
| Nausea<br>subjects affected / exposed<br>occurrences (all)                       | 7 / 10 (70.00%)<br>8 | 4 / 11 (36.36%)<br>5 | 0 / 1 (0.00%)<br>0 |
| Oral pain<br>subjects affected / exposed<br>occurrences (all)                    | 1 / 10 (10.00%)<br>1 | 0 / 11 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0 |
| Stomatitis<br>subjects affected / exposed<br>occurrences (all)                   | 0 / 10 (0.00%)<br>0  | 0 / 11 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0 |
| Vomiting<br>subjects affected / exposed<br>occurrences (all)                     | 3 / 10 (30.00%)<br>3 | 1 / 11 (9.09%)<br>1  | 0 / 1 (0.00%)<br>0 |
| Abdominal tenderness<br>subjects affected / exposed<br>occurrences (all)         | 0 / 10 (0.00%)<br>0  | 0 / 11 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0 |
| Aphthous ulcer<br>subjects affected / exposed<br>occurrences (all)               | 0 / 10 (0.00%)<br>0  | 0 / 11 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0 |
| Autoimmune colitis<br>subjects affected / exposed<br>occurrences (all)           | 0 / 10 (0.00%)<br>0  | 0 / 11 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0 |
| Ascites<br>subjects affected / exposed<br>occurrences (all)                      | 0 / 10 (0.00%)<br>0  | 0 / 11 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0 |
| Chronic gastritis<br>subjects affected / exposed<br>occurrences (all)            | 0 / 10 (0.00%)<br>0  | 0 / 11 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0 |
| Faecaloma<br>subjects affected / exposed<br>occurrences (all)                    | 0 / 10 (0.00%)<br>0  | 0 / 11 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0 |



|  |                      |                      |                    |
|--|----------------------|----------------------|--------------------|
| Gastrooesophageal reflux disease<br>subjects affected / exposed<br>occurrences (all)   | 0 / 10 (0.00%)<br>0  | 0 / 11 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0 |
| Hepatobiliary disorders  |                      |                      |                    |
| Hepatic pain<br>subjects affected / exposed<br>occurrences (all)                       | 0 / 10 (0.00%)<br>0  | 2 / 11 (18.18%)<br>2 | 0 / 1 (0.00%)<br>0 |
| Hypertransaminasaemia<br>subjects affected / exposed<br>occurrences (all)              | 0 / 10 (0.00%)<br>0  | 0 / 11 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0 |
| Bile duct obstruction<br>subjects affected / exposed<br>occurrences (all)              | 0 / 10 (0.00%)<br>0  | 0 / 11 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0 |
| Cholelithiasis<br>subjects affected / exposed<br>occurrences (all)                     | 0 / 10 (0.00%)<br>0  | 0 / 11 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0 |
| Skin and subcutaneous tissue disorders   |                      |                      |                    |
| Alopecia<br>subjects affected / exposed<br>occurrences (all)                           | 1 / 10 (10.00%)<br>1 | 0 / 11 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0 |
| Actinic keratosis<br>subjects affected / exposed<br>occurrences (all)                  | 1 / 10 (10.00%)<br>1 | 0 / 11 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0 |
| Dermatitis acneiform<br>subjects affected / exposed<br>occurrences (all)               | 1 / 10 (10.00%)<br>2 | 0 / 11 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0 |
| Dry skin<br>subjects affected / exposed<br>occurrences (all)                           | 1 / 10 (10.00%)<br>1 | 2 / 11 (18.18%)<br>2 | 0 / 1 (0.00%)<br>0 |
| Dermatitis exfoliative generalised<br>subjects affected / exposed<br>occurrences (all) | 1 / 10 (10.00%)<br>1 | 0 / 11 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0 |
| Hyperhidrosis<br>subjects affected / exposed<br>occurrences (all)                      | 0 / 10 (0.00%)<br>0  | 0 / 11 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0 |
| Eczema nummular  |                      |                      |                    |

|                             |                 |                |               |
|-----------------------------|-----------------|----------------|---------------|
| subjects affected / exposed | 0 / 10 (0.00%)  | 0 / 11 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 0               | 0              | 0             |
| Lichenoid keratosis         |                 |                |               |
| subjects affected / exposed | 0 / 10 (0.00%)  | 0 / 11 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 0               | 0              | 0             |
| Livedo reticularis          |                 |                |               |
| subjects affected / exposed | 1 / 10 (10.00%) | 0 / 11 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 1               | 0              | 0             |
| Pruritus                    |                 |                |               |
| subjects affected / exposed | 4 / 10 (40.00%) | 1 / 11 (9.09%) | 0 / 1 (0.00%) |
| occurrences (all)           | 4               | 1              | 0             |
| Rash                        |                 |                |               |
| subjects affected / exposed | 1 / 10 (10.00%) | 1 / 11 (9.09%) | 0 / 1 (0.00%) |
| occurrences (all)           | 1               | 1              | 0             |
| Rash erythematous           |                 |                |               |
| subjects affected / exposed | 0 / 10 (0.00%)  | 1 / 11 (9.09%) | 0 / 1 (0.00%) |
| occurrences (all)           | 0               | 1              | 0             |
| Rash maculo-papular         |                 |                |               |
| subjects affected / exposed | 1 / 10 (10.00%) | 0 / 11 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 1               | 0              | 0             |
| Rash papular                |                 |                |               |
| subjects affected / exposed | 1 / 10 (10.00%) | 1 / 11 (9.09%) | 0 / 1 (0.00%) |
| occurrences (all)           | 1               | 1              | 0             |
| Rash pruritic               |                 |                |               |
| subjects affected / exposed | 0 / 10 (0.00%)  | 0 / 11 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 0               | 0              | 0             |
| Scab                        |                 |                |               |
| subjects affected / exposed | 1 / 10 (10.00%) | 0 / 11 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 1               | 0              | 0             |
| Skin hypopigmentation       |                 |                |               |
| subjects affected / exposed | 2 / 10 (20.00%) | 0 / 11 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 2               | 0              | 0             |
| Vitiligo                    |                 |                |               |
| subjects affected / exposed | 0 / 10 (0.00%)  | 1 / 11 (9.09%) | 0 / 1 (0.00%) |
| occurrences (all)           | 0               | 1              | 0             |
| Erythema                    |                 |                |               |

|                             |                |                |               |
|-----------------------------|----------------|----------------|---------------|
| subjects affected / exposed | 0 / 10 (0.00%) | 0 / 11 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 0              | 0              | 0             |
| Night sweats                |                |                |               |
| subjects affected / exposed | 0 / 10 (0.00%) | 0 / 11 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 0              | 0              | 0             |
| Scar pain                   |                |                |               |
| subjects affected / exposed | 0 / 10 (0.00%) | 0 / 11 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 0              | 0              | 0             |
| Skin ulcer                  |                |                |               |
| subjects affected / exposed | 0 / 10 (0.00%) | 0 / 11 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 0              | 0              | 0             |
| Facial wasting              |                |                |               |
| subjects affected / exposed | 0 / 10 (0.00%) | 0 / 11 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 0              | 0              | 0             |
| Renal and urinary disorders |                |                |               |
| Chromaturia                 |                |                |               |
| subjects affected / exposed | 0 / 10 (0.00%) | 0 / 11 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 0              | 0              | 0             |
| Acute kidney injury         |                |                |               |
| subjects affected / exposed | 0 / 10 (0.00%) | 0 / 11 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 0              | 0              | 0             |
| Dysuria                     |                |                |               |
| subjects affected / exposed | 0 / 10 (0.00%) | 0 / 11 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 0              | 0              | 0             |
| Pollakiuria                 |                |                |               |
| subjects affected / exposed | 0 / 10 (0.00%) | 0 / 11 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 0              | 0              | 0             |
| Haematuria                  |                |                |               |
| subjects affected / exposed | 0 / 10 (0.00%) | 0 / 11 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 0              | 0              | 0             |
| Nocturia                    |                |                |               |
| subjects affected / exposed | 0 / 10 (0.00%) | 0 / 11 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 0              | 0              | 0             |
| Polyuria                    |                |                |               |
| subjects affected / exposed | 0 / 10 (0.00%) | 0 / 11 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 0              | 0              | 0             |

|   |                      |                     |                    |
|---|----------------------|---------------------|--------------------|
| Urinary hesitation<br>subjects affected / exposed<br>occurrences (all)    | 0 / 10 (0.00%)<br>0  | 0 / 11 (0.00%)<br>0 | 0 / 1 (0.00%)<br>0 |
| Urinary incontinence<br>subjects affected / exposed<br>occurrences (all)  | 0 / 10 (0.00%)<br>0  | 0 / 11 (0.00%)<br>0 | 0 / 1 (0.00%)<br>0 |
| Endocrine disorders   |                      |                     |                    |
| Adrenal insufficiency<br>subjects affected / exposed<br>occurrences (all) | 3 / 10 (30.00%)<br>3 | 0 / 11 (0.00%)<br>0 | 0 / 1 (0.00%)<br>0 |
| Endocrine disorder<br>subjects affected / exposed<br>occurrences (all)    | 0 / 10 (0.00%)<br>0  | 0 / 11 (0.00%)<br>0 | 0 / 1 (0.00%)<br>0 |
| Hyperthyroidism<br>subjects affected / exposed<br>occurrences (all)       | 1 / 10 (10.00%)<br>1 | 0 / 11 (0.00%)<br>0 | 0 / 1 (0.00%)<br>0 |
| Hypophysitis<br>subjects affected / exposed<br>occurrences (all)          | 0 / 10 (0.00%)<br>0  | 0 / 11 (0.00%)<br>0 | 0 / 1 (0.00%)<br>0 |
| Hypothyroidism<br>subjects affected / exposed<br>occurrences (all)        | 3 / 10 (30.00%)<br>3 | 0 / 11 (0.00%)<br>0 | 0 / 1 (0.00%)<br>0 |
| Thyroiditis<br>subjects affected / exposed<br>occurrences (all)           | 1 / 10 (10.00%)<br>1 | 0 / 11 (0.00%)<br>0 | 0 / 1 (0.00%)<br>0 |
| Musculoskeletal and connective tissue disorders                           |                      |                     |                    |
| Arthralgia<br>subjects affected / exposed<br>occurrences (all)            | 3 / 10 (30.00%)<br>3 | 1 / 11 (9.09%)<br>1 | 0 / 1 (0.00%)<br>0 |
| Arthritis<br>subjects affected / exposed<br>occurrences (all)             | 1 / 10 (10.00%)<br>1 | 0 / 11 (0.00%)<br>0 | 0 / 1 (0.00%)<br>0 |
| Back pain<br>subjects affected / exposed<br>occurrences (all)             | 1 / 10 (10.00%)<br>1 | 0 / 11 (0.00%)<br>0 | 0 / 1 (0.00%)<br>0 |
| Bone pain   |                      |                     |                    |

|                                 |                 |                 |               |
|---------------------------------|-----------------|-----------------|---------------|
| subjects affected / exposed     | 1 / 10 (10.00%) | 0 / 11 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)               | 1               | 0               | 0             |
| Flank pain                      |                 |                 |               |
| subjects affected / exposed     | 1 / 10 (10.00%) | 0 / 11 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)               | 1               | 0               | 0             |
| Joint range of motion decreased |                 |                 |               |
| subjects affected / exposed     | 1 / 10 (10.00%) | 0 / 11 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)               | 1               | 0               | 0             |
| Muscle spasms                   |                 |                 |               |
| subjects affected / exposed     | 0 / 10 (0.00%)  | 0 / 11 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)               | 0               | 0               | 0             |
| Musculoskeletal pain            |                 |                 |               |
| subjects affected / exposed     | 2 / 10 (20.00%) | 0 / 11 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)               | 3               | 0               | 0             |
| Muscular weakness               |                 |                 |               |
| subjects affected / exposed     | 1 / 10 (10.00%) | 0 / 11 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)               | 1               | 0               | 0             |
| Neck pain                       |                 |                 |               |
| subjects affected / exposed     | 0 / 10 (0.00%)  | 0 / 11 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)               | 0               | 0               | 0             |
| Myalgia                         |                 |                 |               |
| subjects affected / exposed     | 1 / 10 (10.00%) | 0 / 11 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)               | 1               | 0               | 0             |
| Pain in extremity               |                 |                 |               |
| subjects affected / exposed     | 2 / 10 (20.00%) | 3 / 11 (27.27%) | 0 / 1 (0.00%) |
| occurrences (all)               | 3               | 3               | 0             |
| Pain in jaw                     |                 |                 |               |
| subjects affected / exposed     | 1 / 10 (10.00%) | 0 / 11 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)               | 1               | 0               | 0             |
| Musculoskeletal stiffness       |                 |                 |               |
| subjects affected / exposed     | 0 / 10 (0.00%)  | 0 / 11 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)               | 0               | 0               | 0             |
| Infections and infestations     |                 |                 |               |
| Candida infection               |                 |                 |               |
| subjects affected / exposed     | 0 / 10 (0.00%)  | 0 / 11 (0.00%)  | 0 / 1 (0.00%) |
| occurrences (all)               | 0               | 0               | 0             |

|                             |                 |                |               |
|-----------------------------|-----------------|----------------|---------------|
| Cellulitis                  |                 |                |               |
| subjects affected / exposed | 0 / 10 (0.00%)  | 1 / 11 (9.09%) | 0 / 1 (0.00%) |
| occurrences (all)           | 0               | 1              | 0             |
| Conjunctivitis              |                 |                |               |
| subjects affected / exposed | 2 / 10 (20.00%) | 0 / 11 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 2               | 0              | 0             |
| Influenza                   |                 |                |               |
| subjects affected / exposed | 1 / 10 (10.00%) | 0 / 11 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 1               | 0              | 0             |
| Cytomegalovirus infection   |                 |                |               |
| subjects affected / exposed | 1 / 10 (10.00%) | 0 / 11 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 1               | 0              | 0             |
| Pneumonia                   |                 |                |               |
| subjects affected / exposed | 1 / 10 (10.00%) | 0 / 11 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 1               | 0              | 0             |
| Nasopharyngitis             |                 |                |               |
| subjects affected / exposed | 0 / 10 (0.00%)  | 0 / 11 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 0               | 0              | 0             |
| Rash pustular               |                 |                |               |
| subjects affected / exposed | 2 / 10 (20.00%) | 0 / 11 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 2               | 0              | 0             |
| Respiratory tract infection |                 |                |               |
| subjects affected / exposed | 0 / 10 (0.00%)  | 1 / 11 (9.09%) | 0 / 1 (0.00%) |
| occurrences (all)           | 0               | 1              | 0             |
| Rhinitis                    |                 |                |               |
| subjects affected / exposed | 2 / 10 (20.00%) | 0 / 11 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 2               | 0              | 0             |
| Sepsis                      |                 |                |               |
| subjects affected / exposed | 0 / 10 (0.00%)  | 0 / 11 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 0               | 0              | 0             |
| Sinusitis                   |                 |                |               |
| subjects affected / exposed | 0 / 10 (0.00%)  | 0 / 11 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 0               | 0              | 0             |
| Skin infection              |                 |                |               |
| subjects affected / exposed | 0 / 10 (0.00%)  | 0 / 11 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 0               | 0              | 0             |

|  |                 |                |               |
|--|-----------------|----------------|---------------|
| Upper respiratory tract infection<br>subjects affected / exposed | 1 / 10 (10.00%) | 0 / 11 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)  | 2               | 0              | 0             |
| Urinary tract infection<br>subjects affected / exposed           | 1 / 10 (10.00%) | 0 / 11 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)  | 1               | 0              | 0             |
| Fungal skin infection<br>subjects affected / exposed             | 0 / 10 (0.00%)  | 0 / 11 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)  | 0               | 0              | 0             |
| Hordeolum<br>subjects affected / exposed                         | 0 / 10 (0.00%)  | 0 / 11 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)  | 0               | 0              | 0             |
| Infected skin ulcer<br>subjects affected / exposed               | 0 / 10 (0.00%)  | 0 / 11 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)  | 0               | 0              | 0             |
| Laryngitis<br>subjects affected / exposed                        | 0 / 10 (0.00%)  | 0 / 11 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)  | 0               | 0              | 0             |
| Onychomycosis<br>subjects affected / exposed                     | 0 / 10 (0.00%)  | 0 / 11 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)  | 0               | 0              | 0             |
| Oral candidiasis<br>subjects affected / exposed                  | 0 / 10 (0.00%)  | 0 / 11 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)  | 0               | 0              | 0             |
| Oral herpes<br>subjects affected / exposed                       | 0 / 10 (0.00%)  | 0 / 11 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)  | 0               | 0              | 0             |
| Pyuria<br>subjects affected / exposed                            | 0 / 10 (0.00%)  | 0 / 11 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)  | 0               | 0              | 0             |
| Staphylococcal infection<br>subjects affected / exposed          | 0 / 10 (0.00%)  | 0 / 11 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)  | 0               | 0              | 0             |
| Herpes zoster<br>subjects affected / exposed                     | 0 / 10 (0.00%)  | 0 / 11 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)  | 0               | 0              | 0             |

|                                    |                 |                |                 |
|------------------------------------|-----------------|----------------|-----------------|
| Metabolism and nutrition disorders |                 |                |                 |
| Decreased appetite                 |                 |                |                 |
| subjects affected / exposed        | 4 / 10 (40.00%) | 1 / 11 (9.09%) | 1 / 1 (100.00%) |
| occurrences (all)                  | 4               | 1              | 1               |
| Dehydration                        |                 |                |                 |
| subjects affected / exposed        | 1 / 10 (10.00%) | 0 / 11 (0.00%) | 0 / 1 (0.00%)   |
| occurrences (all)                  | 1               | 0              | 0               |
| Hypercalcaemia                     |                 |                |                 |
| subjects affected / exposed        | 0 / 10 (0.00%)  | 0 / 11 (0.00%) | 0 / 1 (0.00%)   |
| occurrences (all)                  | 0               | 0              | 0               |
| Hyperglycaemia                     |                 |                |                 |
| subjects affected / exposed        | 1 / 10 (10.00%) | 1 / 11 (9.09%) | 0 / 1 (0.00%)   |
| occurrences (all)                  | 2               | 1              | 0               |
| Hyperuricaemia                     |                 |                |                 |
| subjects affected / exposed        | 1 / 10 (10.00%) | 0 / 11 (0.00%) | 0 / 1 (0.00%)   |
| occurrences (all)                  | 1               | 0              | 0               |
| Hypoalbuminaemia                   |                 |                |                 |
| subjects affected / exposed        | 0 / 10 (0.00%)  | 0 / 11 (0.00%) | 0 / 1 (0.00%)   |
| occurrences (all)                  | 0               | 0              | 0               |
| Hypoglycaemia                      |                 |                |                 |
| subjects affected / exposed        | 0 / 10 (0.00%)  | 0 / 11 (0.00%) | 0 / 1 (0.00%)   |
| occurrences (all)                  | 0               | 0              | 0               |
| Hypokalaemia                       |                 |                |                 |
| subjects affected / exposed        | 0 / 10 (0.00%)  | 0 / 11 (0.00%) | 0 / 1 (0.00%)   |
| occurrences (all)                  | 0               | 0              | 0               |
| Hypomagnesaemia                    |                 |                |                 |
| subjects affected / exposed        | 0 / 10 (0.00%)  | 0 / 11 (0.00%) | 0 / 1 (0.00%)   |
| occurrences (all)                  | 0               | 0              | 0               |
| Hyponatraemia                      |                 |                |                 |
| subjects affected / exposed        | 1 / 10 (10.00%) | 0 / 11 (0.00%) | 0 / 1 (0.00%)   |
| occurrences (all)                  | 1               | 0              | 0               |
| Hypophosphataemia                  |                 |                |                 |
| subjects affected / exposed        | 0 / 10 (0.00%)  | 0 / 11 (0.00%) | 0 / 1 (0.00%)   |
| occurrences (all)                  | 0               | 0              | 0               |
| Lactic acidosis                    |                 |                |                 |



|                             |                |                |               |
|-----------------------------|----------------|----------------|---------------|
| subjects affected / exposed | 0 / 10 (0.00%) | 0 / 11 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 0              | 0              | 0             |
| Malnutrition                |                |                |               |
| subjects affected / exposed | 0 / 10 (0.00%) | 0 / 11 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 0              | 0              | 0             |
| Diabetes mellitus           |                |                |               |
| subjects affected / exposed | 0 / 10 (0.00%) | 0 / 11 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 0              | 0              | 0             |
| Fluid retention             |                |                |               |
| subjects affected / exposed | 0 / 10 (0.00%) | 0 / 11 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 0              | 0              | 0             |
| Hyperkalaemia               |                |                |               |
| subjects affected / exposed | 0 / 10 (0.00%) | 0 / 11 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 0              | 0              | 0             |
| Hypocalcaemia               |                |                |               |
| subjects affected / exposed | 0 / 10 (0.00%) | 0 / 11 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 0              | 0              | 0             |
| Hypophagia                  |                |                |               |
| subjects affected / exposed | 0 / 10 (0.00%) | 0 / 11 (0.00%) | 0 / 1 (0.00%) |
| occurrences (all)           | 0              | 0              | 0             |

| <b>Non-serious adverse events</b>                                   | N3 30M BM       | Unplanned Treatment |  |
|---|-----------------|---------------------|--|
| Total subjects affected by non-serious adverse events               |                 |                     |  |
| subjects affected / exposed   | 9 / 10 (90.00%) | 1 / 1 (100.00%)     |  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                 |                     |  |
| Malignant neoplasm progression                                      |                 |                     |  |
| subjects affected / exposed   | 1 / 10 (10.00%) | 0 / 1 (0.00%)       |  |
| occurrences (all)   | 1               | 0                   |  |
| Tumour pain   |                 |                     |  |
| subjects affected / exposed   | 0 / 10 (0.00%)  | 0 / 1 (0.00%)       |  |
| occurrences (all)   | 0               | 0                   |  |
| Tumour embolism   |                 |                     |  |
| subjects affected / exposed   | 0 / 10 (0.00%)  | 0 / 1 (0.00%)       |  |
| occurrences (all)   | 0               | 0                   |  |
| Oncologic complication  |                 |                     |  |

|   |                      |                      |  |
|---|----------------------|----------------------|--|
| subjects affected / exposed<br>occurrences (all)        | 0 / 10 (0.00%)<br>0  | 1 / 1 (100.00%)<br>1 |  |
| Vascular disorders                                      |                      |                      |  |
| Embolism  |                      |                      |  |
| subjects affected / exposed<br>occurrences (all)        | 0 / 10 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0   |  |
| Flushing  |                      |                      |  |
| subjects affected / exposed<br>occurrences (all)        | 1 / 10 (10.00%)<br>1 | 0 / 1 (0.00%)<br>0   |  |
| Hypertension  |                      |                      |  |
| subjects affected / exposed<br>occurrences (all)        | 0 / 10 (0.00%)<br>0  | 1 / 1 (100.00%)<br>1 |  |
| Hypotension   |                      |                      |  |
| subjects affected / exposed<br>occurrences (all)        | 0 / 10 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0   |  |
| Lymphoedema   |                      |                      |  |
| subjects affected / exposed<br>occurrences (all)        | 0 / 10 (0.00%)<br>0  | 1 / 1 (100.00%)<br>1 |  |
| Hot flush   |                      |                      |  |
| subjects affected / exposed<br>occurrences (all)        | 0 / 10 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0   |  |
| Orthostatic hypotension                                 |                      |                      |  |
| subjects affected / exposed<br>occurrences (all)        | 0 / 10 (0.00%)<br>0  | 1 / 1 (100.00%)<br>1 |  |
| General disorders and administration<br>site conditions |                      |                      |  |
| Asthenia  |                      |                      |  |
| subjects affected / exposed<br>occurrences (all)        | 0 / 10 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0   |  |
| Chest pain  |                      |                      |  |
| subjects affected / exposed<br>occurrences (all)        | 2 / 10 (20.00%)<br>2 | 1 / 1 (100.00%)<br>1 |  |
| Chills  |                      |                      |  |
| subjects affected / exposed<br>occurrences (all)        | 2 / 10 (20.00%)<br>2 | 0 / 1 (0.00%)<br>0   |  |
| Fatigue   |                      |                      |  |

|                             |                 |                 |
|-----------------------------|-----------------|-----------------|
| subjects affected / exposed | 6 / 10 (60.00%) | 1 / 1 (100.00%) |
| occurrences (all)           | 6               | 2               |
| Hernia pain                 |                 |                 |
| subjects affected / exposed | 1 / 10 (10.00%) | 0 / 1 (0.00%)   |
| occurrences (all)           | 1               | 0               |
| Influenza like illness      |                 |                 |
| subjects affected / exposed | 3 / 10 (30.00%) | 0 / 1 (0.00%)   |
| occurrences (all)           | 3               | 0               |
| Localised oedema            |                 |                 |
| subjects affected / exposed | 0 / 10 (0.00%)  | 0 / 1 (0.00%)   |
| occurrences (all)           | 0               | 0               |
| Malaise                     |                 |                 |
| subjects affected / exposed | 0 / 10 (0.00%)  | 0 / 1 (0.00%)   |
| occurrences (all)           | 0               | 0               |
| Mucosal inflammation        |                 |                 |
| subjects affected / exposed | 0 / 10 (0.00%)  | 0 / 1 (0.00%)   |
| occurrences (all)           | 0               | 0               |
| Non-cardiac chest pain      |                 |                 |
| subjects affected / exposed | 1 / 10 (10.00%) | 0 / 1 (0.00%)   |
| occurrences (all)           | 1               | 0               |
| Oedema peripheral           |                 |                 |
| subjects affected / exposed | 1 / 10 (10.00%) | 0 / 1 (0.00%)   |
| occurrences (all)           | 2               | 0               |
| Pain                        |                 |                 |
| subjects affected / exposed | 1 / 10 (10.00%) | 0 / 1 (0.00%)   |
| occurrences (all)           | 1               | 0               |
| Peripheral swelling         |                 |                 |
| subjects affected / exposed | 0 / 10 (0.00%)  | 0 / 1 (0.00%)   |
| occurrences (all)           | 0               | 0               |
| Pyrexia                     |                 |                 |
| subjects affected / exposed | 3 / 10 (30.00%) | 0 / 1 (0.00%)   |
| occurrences (all)           | 3               | 0               |
| Temperature intolerance     |                 |                 |
| subjects affected / exposed | 0 / 10 (0.00%)  | 0 / 1 (0.00%)   |
| occurrences (all)           | 0               | 0               |
| Decreased activity          |                 |                 |

|  |                 |                 |  |
|--|-----------------|-----------------|--|
| subjects affected / exposed              | 0 / 10 (0.00%)  | 0 / 1 (0.00%)   |  |
| occurrences (all)                        | 0               | 0               |  |
| Feeling cold                             |                 |                 |  |
| subjects affected / exposed              | 0 / 10 (0.00%)  | 0 / 1 (0.00%)   |  |
| occurrences (all)                        | 0               | 0               |  |
| Gait disturbance                         |                 |                 |  |
| subjects affected / exposed              | 0 / 10 (0.00%)  | 0 / 1 (0.00%)   |  |
| occurrences (all)                        | 0               | 0               |  |
| Feeling of body temperature change       |                 |                 |  |
| subjects affected / exposed              | 0 / 10 (0.00%)  | 0 / 1 (0.00%)   |  |
| occurrences (all)                        | 0               | 0               |  |
| Inflammation                             |                 |                 |  |
| subjects affected / exposed              | 0 / 10 (0.00%)  | 0 / 1 (0.00%)   |  |
| occurrences (all)                        | 0               | 0               |  |
| Physical deconditioning                  |                 |                 |  |
| subjects affected / exposed              | 0 / 10 (0.00%)  | 0 / 1 (0.00%)   |  |
| occurrences (all)                        | 0               | 0               |  |
| Axillary pain                            |                 |                 |  |
| subjects affected / exposed              | 0 / 10 (0.00%)  | 1 / 1 (100.00%) |  |
| occurrences (all)                        | 0               | 1               |  |
| Immune system disorders                  |                 |                 |  |
| Drug hypersensitivity                    |                 |                 |  |
| subjects affected / exposed              | 1 / 10 (10.00%) | 0 / 1 (0.00%)   |  |
| occurrences (all)                        | 1               | 0               |  |
| Hypersensitivity                         |                 |                 |  |
| subjects affected / exposed              | 1 / 10 (10.00%) | 0 / 1 (0.00%)   |  |
| occurrences (all)                        | 1               | 0               |  |
| Reproductive system and breast disorders |                 |                 |  |
| Nipple pain                              |                 |                 |  |
| subjects affected / exposed              | 1 / 10 (10.00%) | 0 / 1 (0.00%)   |  |
| occurrences (all)                        | 1               | 0               |  |
| Spermatic cord haemorrhage               |                 |                 |  |
| subjects affected / exposed              | 0 / 10 (0.00%)  | 0 / 1 (0.00%)   |  |
| occurrences (all)                        | 0               | 0               |  |
| Genital rash                             |                 |                 |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 0 / 1 (0.00%)   |  |
| occurrences (all)                               | 0               | 0               |  |
| Scrotal swelling                                |                 |                 |  |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 0 / 1 (0.00%)   |  |
| occurrences (all)                               | 0               | 0               |  |
| Respiratory, thoracic and mediastinal disorders |                 |                 |  |
| Bronchial obstruction                           |                 |                 |  |
| subjects affected / exposed                     | 1 / 10 (10.00%) | 0 / 1 (0.00%)   |  |
| occurrences (all)                               | 1               | 0               |  |
| Cough   |                 |                 |  |
| subjects affected / exposed                     | 3 / 10 (30.00%) | 1 / 1 (100.00%) |  |
| occurrences (all)                               | 4               | 1               |  |
| Dyspnoea  |                 |                 |  |
| subjects affected / exposed                     | 2 / 10 (20.00%) | 1 / 1 (100.00%) |  |
| occurrences (all)                               | 2               | 1               |  |
| Hypoxia   |                 |                 |  |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 0 / 1 (0.00%)   |  |
| occurrences (all)                               | 0               | 0               |  |
| Oropharyngeal pain                              |                 |                 |  |
| subjects affected / exposed                     | 1 / 10 (10.00%) | 0 / 1 (0.00%)   |  |
| occurrences (all)                               | 1               | 0               |  |
| Nasal congestion                                |                 |                 |  |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 0 / 1 (0.00%)   |  |
| occurrences (all)                               | 0               | 0               |  |
| Pleural effusion                                |                 |                 |  |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 0 / 1 (0.00%)   |  |
| occurrences (all)                               | 0               | 0               |  |
| Pneumonitis                                     |                 |                 |  |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 0 / 1 (0.00%)   |  |
| occurrences (all)                               | 0               | 0               |  |
| Productive cough                                |                 |                 |  |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 0 / 1 (0.00%)   |  |
| occurrences (all)                               | 0               | 0               |  |
| Rhinitis allergic                               |                 |                 |  |

|                              |                |               |  |
|------------------------------|----------------|---------------|--|
| subjects affected / exposed  | 0 / 10 (0.00%) | 0 / 1 (0.00%) |  |
| occurrences (all)            | 0              | 0             |  |
| Rhinorrhoea                  |                |               |  |
| subjects affected / exposed  | 0 / 10 (0.00%) | 0 / 1 (0.00%) |  |
| occurrences (all)            | 0              | 0             |  |
| Upper-airway cough syndrome  |                |               |  |
| subjects affected / exposed  | 0 / 10 (0.00%) | 0 / 1 (0.00%) |  |
| occurrences (all)            | 0              | 0             |  |
| Dysphonia                    |                |               |  |
| subjects affected / exposed  | 0 / 10 (0.00%) | 0 / 1 (0.00%) |  |
| occurrences (all)            | 0              | 0             |  |
| Dyspnoea exertional          |                |               |  |
| subjects affected / exposed  | 0 / 10 (0.00%) | 0 / 1 (0.00%) |  |
| occurrences (all)            | 0              | 0             |  |
| Epistaxis                    |                |               |  |
| subjects affected / exposed  | 0 / 10 (0.00%) | 0 / 1 (0.00%) |  |
| occurrences (all)            | 0              | 0             |  |
| Haemoptysis                  |                |               |  |
| subjects affected / exposed  | 0 / 10 (0.00%) | 0 / 1 (0.00%) |  |
| occurrences (all)            | 0              | 0             |  |
| Hiccups                      |                |               |  |
| subjects affected / exposed  | 0 / 10 (0.00%) | 0 / 1 (0.00%) |  |
| occurrences (all)            | 0              | 0             |  |
| Pulmonary embolism           |                |               |  |
| subjects affected / exposed  | 0 / 10 (0.00%) | 0 / 1 (0.00%) |  |
| occurrences (all)            | 0              | 0             |  |
| Respiratory failure          |                |               |  |
| subjects affected / exposed  | 0 / 10 (0.00%) | 0 / 1 (0.00%) |  |
| occurrences (all)            | 0              | 0             |  |
| Respiratory tract congestion |                |               |  |
| subjects affected / exposed  | 0 / 10 (0.00%) | 0 / 1 (0.00%) |  |
| occurrences (all)            | 0              | 0             |  |
| Psychiatric disorders        |                |               |  |
| Confusional state            |                |               |  |
| subjects affected / exposed  | 0 / 10 (0.00%) | 0 / 1 (0.00%) |  |
| occurrences (all)            | 0              | 0             |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| Anxiety   |                 |                 |  |
| subjects affected / exposed                     | 1 / 10 (10.00%) | 1 / 1 (100.00%) |  |
| occurrences (all)                               | 1               | 1               |  |
| Depression                                      |                 |                 |  |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 1 / 1 (100.00%) |  |
| occurrences (all)                               | 0               | 1               |  |
| Insomnia  |                 |                 |  |
| subjects affected / exposed                     | 1 / 10 (10.00%) | 1 / 1 (100.00%) |  |
| occurrences (all)                               | 1               | 1               |  |
| Sleep disorder                                  |                 |                 |  |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 0 / 1 (0.00%)   |  |
| occurrences (all)                               | 0               | 0               |  |
| Depressed mood                                  |                 |                 |  |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 0 / 1 (0.00%)   |  |
| occurrences (all)                               | 0               | 0               |  |
| Disorientation                                  |                 |                 |  |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 0 / 1 (0.00%)   |  |
| occurrences (all)                               | 0               | 0               |  |
| Irritability                                    |                 |                 |  |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 0 / 1 (0.00%)   |  |
| occurrences (all)                               | 0               | 0               |  |
| Hallucination                                   |                 |                 |  |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 0 / 1 (0.00%)   |  |
| occurrences (all)                               | 0               | 0               |  |
| Mental status changes                           |                 |                 |  |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 1 / 1 (100.00%) |  |
| occurrences (all)                               | 0               | 1               |  |
| Investigations                                  |                 |                 |  |
| Activated partial thromboplastin time prolonged |                 |                 |  |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 0 / 1 (0.00%)   |  |
| occurrences (all)                               | 0               | 0               |  |
| Alanine aminotransferase increased              |                 |                 |  |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 0 / 1 (0.00%)   |  |
| occurrences (all)                               | 0               | 0               |  |
| Amylase increased                               |                 |                 |  |

|   |                 |               |  |
|---|-----------------|---------------|--|
| subjects affected / exposed                 | 1 / 10 (10.00%) | 0 / 1 (0.00%) |  |
| occurrences (all)                           | 4               | 0             |  |
| Aspartate aminotransferase increased        |                 |               |  |
| subjects affected / exposed                 | 1 / 10 (10.00%) | 0 / 1 (0.00%) |  |
| occurrences (all)                           | 1               | 0             |  |
| Blood alkaline phosphatase increased        |                 |               |  |
| subjects affected / exposed                 | 0 / 10 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences (all)                           | 0               | 0             |  |
| Blood bilirubin increased                   |                 |               |  |
| subjects affected / exposed                 | 0 / 10 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences (all)                           | 0               | 0             |  |
| Blood creatinine increased                  |                 |               |  |
| subjects affected / exposed                 | 1 / 10 (10.00%) | 0 / 1 (0.00%) |  |
| occurrences (all)                           | 4               | 0             |  |
| Blood thyroid stimulating hormone decreased |                 |               |  |
| subjects affected / exposed                 | 2 / 10 (20.00%) | 0 / 1 (0.00%) |  |
| occurrences (all)                           | 2               | 0             |  |
| Blood thyroid stimulating hormone increased |                 |               |  |
| subjects affected / exposed                 | 2 / 10 (20.00%) | 0 / 1 (0.00%) |  |
| occurrences (all)                           | 2               | 0             |  |
| Cortisol increased                          |                 |               |  |
| subjects affected / exposed                 | 0 / 10 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences (all)                           | 0               | 0             |  |
| Hepatic enzyme increased                    |                 |               |  |
| subjects affected / exposed                 | 0 / 10 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences (all)                           | 0               | 0             |  |
| International normalised ratio increased    |                 |               |  |
| subjects affected / exposed                 | 0 / 10 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences (all)                           | 0               | 0             |  |
| Lipase increased                            |                 |               |  |
| subjects affected / exposed                 | 1 / 10 (10.00%) | 0 / 1 (0.00%) |  |
| occurrences (all)                           | 8               | 0             |  |
| Lymphocyte count decreased                  |                 |               |  |



|  |                 |                 |  |
|--|-----------------|-----------------|--|
| subjects affected / exposed                    | 0 / 10 (0.00%)  | 0 / 1 (0.00%)   |  |
| occurrences (all)                              | 0               | 0               |  |
| Platelet count decreased                       |                 |                 |  |
| subjects affected / exposed                    | 1 / 10 (10.00%) | 0 / 1 (0.00%)   |  |
| occurrences (all)                              | 1               | 0               |  |
| Norovirus test positive                        |                 |                 |  |
| subjects affected / exposed                    | 0 / 10 (0.00%)  | 0 / 1 (0.00%)   |  |
| occurrences (all)                              | 0               | 0               |  |
| Transaminases increased                        |                 |                 |  |
| subjects affected / exposed                    | 0 / 10 (0.00%)  | 0 / 1 (0.00%)   |  |
| occurrences (all)                              | 0               | 0               |  |
| Weight decreased                               |                 |                 |  |
| subjects affected / exposed                    | 1 / 10 (10.00%) | 1 / 1 (100.00%) |  |
| occurrences (all)                              | 1               | 1               |  |
| Weight increased                               |                 |                 |  |
| subjects affected / exposed                    | 0 / 10 (0.00%)  | 0 / 1 (0.00%)   |  |
| occurrences (all)                              | 0               | 0               |  |
| Blood urea increased                           |                 |                 |  |
| subjects affected / exposed                    | 0 / 10 (0.00%)  | 0 / 1 (0.00%)   |  |
| occurrences (all)                              | 0               | 0               |  |
| Heart rate increased                           |                 |                 |  |
| subjects affected / exposed                    | 0 / 10 (0.00%)  | 0 / 1 (0.00%)   |  |
| occurrences (all)                              | 0               | 0               |  |
| Injury, poisoning and procedural complications |                 |                 |  |
| Contusion                                      |                 |                 |  |
| subjects affected / exposed                    | 0 / 10 (0.00%)  | 0 / 1 (0.00%)   |  |
| occurrences (all)                              | 0               | 0               |  |
| Infusion related reaction                      |                 |                 |  |
| subjects affected / exposed                    | 1 / 10 (10.00%) | 0 / 1 (0.00%)   |  |
| occurrences (all)                              | 1               | 0               |  |
| Limb injury                                    |                 |                 |  |
| subjects affected / exposed                    | 1 / 10 (10.00%) | 0 / 1 (0.00%)   |  |
| occurrences (all)                              | 1               | 0               |  |
| Procedural pain                                |                 |                 |  |

|                                      |                 |                 |  |
|--------------------------------------|-----------------|-----------------|--|
| subjects affected / exposed          | 1 / 10 (10.00%) | 0 / 1 (0.00%)   |  |
| occurrences (all)                    | 1               | 0               |  |
| Bone fissure                         |                 |                 |  |
| subjects affected / exposed          | 0 / 10 (0.00%)  | 0 / 1 (0.00%)   |  |
| occurrences (all)                    | 0               | 0               |  |
| Radiation pneumonitis                |                 |                 |  |
| subjects affected / exposed          | 0 / 10 (0.00%)  | 0 / 1 (0.00%)   |  |
| occurrences (all)                    | 0               | 0               |  |
| Fall                                 |                 |                 |  |
| subjects affected / exposed          | 0 / 10 (0.00%)  | 1 / 1 (100.00%) |  |
| occurrences (all)                    | 0               | 2               |  |
| Cardiac disorders                    |                 |                 |  |
| Acute coronary syndrome              |                 |                 |  |
| subjects affected / exposed          | 0 / 10 (0.00%)  | 0 / 1 (0.00%)   |  |
| occurrences (all)                    | 0               | 0               |  |
| Angina pectoris                      |                 |                 |  |
| subjects affected / exposed          | 1 / 10 (10.00%) | 0 / 1 (0.00%)   |  |
| occurrences (all)                    | 1               | 0               |  |
| Palpitations                         |                 |                 |  |
| subjects affected / exposed          | 0 / 10 (0.00%)  | 0 / 1 (0.00%)   |  |
| occurrences (all)                    | 0               | 0               |  |
| Tachycardia                          |                 |                 |  |
| subjects affected / exposed          | 0 / 10 (0.00%)  | 0 / 1 (0.00%)   |  |
| occurrences (all)                    | 0               | 0               |  |
| Cardiac failure congestive           |                 |                 |  |
| subjects affected / exposed          | 0 / 10 (0.00%)  | 0 / 1 (0.00%)   |  |
| occurrences (all)                    | 0               | 0               |  |
| Atrioventricular block second degree |                 |                 |  |
| subjects affected / exposed          | 0 / 10 (0.00%)  | 0 / 1 (0.00%)   |  |
| occurrences (all)                    | 0               | 0               |  |
| Nervous system disorders             |                 |                 |  |
| Autonomic nervous system imbalance   |                 |                 |  |
| subjects affected / exposed          | 0 / 10 (0.00%)  | 0 / 1 (0.00%)   |  |
| occurrences (all)                    | 0               | 0               |  |
| Cerebrovascular accident             |                 |                 |  |

|                             |                 |                 |  |
|-----------------------------|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 10 (0.00%)  | 0 / 1 (0.00%)   |  |
| occurrences (all)           | 0               | 0               |  |
| Disturbance in attention    |                 |                 |  |
| subjects affected / exposed | 1 / 10 (10.00%) | 0 / 1 (0.00%)   |  |
| occurrences (all)           | 1               | 0               |  |
| Dizziness                   |                 |                 |  |
| subjects affected / exposed | 2 / 10 (20.00%) | 0 / 1 (0.00%)   |  |
| occurrences (all)           | 3               | 0               |  |
| Dysaesthesia                |                 |                 |  |
| subjects affected / exposed | 4 / 10 (40.00%) | 0 / 1 (0.00%)   |  |
| occurrences (all)           | 4               | 0               |  |
| Dysarthria                  |                 |                 |  |
| subjects affected / exposed | 0 / 10 (0.00%)  | 0 / 1 (0.00%)   |  |
| occurrences (all)           | 0               | 0               |  |
| Dysgeusia                   |                 |                 |  |
| subjects affected / exposed | 1 / 10 (10.00%) | 0 / 1 (0.00%)   |  |
| occurrences (all)           | 1               | 0               |  |
| Headache                    |                 |                 |  |
| subjects affected / exposed | 2 / 10 (20.00%) | 0 / 1 (0.00%)   |  |
| occurrences (all)           | 2               | 0               |  |
| Hemiparesis                 |                 |                 |  |
| subjects affected / exposed | 1 / 10 (10.00%) | 0 / 1 (0.00%)   |  |
| occurrences (all)           | 1               | 0               |  |
| Lethargy                    |                 |                 |  |
| subjects affected / exposed | 0 / 10 (0.00%)  | 1 / 1 (100.00%) |  |
| occurrences (all)           | 0               | 1               |  |
| Neuropathy peripheral       |                 |                 |  |
| subjects affected / exposed | 0 / 10 (0.00%)  | 0 / 1 (0.00%)   |  |
| occurrences (all)           | 0               | 0               |  |
| Paraesthesia                |                 |                 |  |
| subjects affected / exposed | 1 / 10 (10.00%) | 0 / 1 (0.00%)   |  |
| occurrences (all)           | 1               | 0               |  |
| Presyncope                  |                 |                 |  |
| subjects affected / exposed | 0 / 10 (0.00%)  | 0 / 1 (0.00%)   |  |
| occurrences (all)           | 0               | 0               |  |
| Restless legs syndrome      |                 |                 |  |

|                             |                |               |  |
|-----------------------------|----------------|---------------|--|
| subjects affected / exposed | 0 / 10 (0.00%) | 0 / 1 (0.00%) |  |
| occurrences (all)           | 0              | 0             |  |
| Seizure                     |                |               |  |
| subjects affected / exposed | 0 / 10 (0.00%) | 0 / 1 (0.00%) |  |
| occurrences (all)           | 0              | 0             |  |
| Aphasia                     |                |               |  |
| subjects affected / exposed | 0 / 10 (0.00%) | 0 / 1 (0.00%) |  |
| occurrences (all)           | 0              | 0             |  |
| Amnesia                     |                |               |  |
| subjects affected / exposed | 0 / 10 (0.00%) | 0 / 1 (0.00%) |  |
| occurrences (all)           | 0              | 0             |  |
| Fine motor delay            |                |               |  |
| subjects affected / exposed | 0 / 10 (0.00%) | 0 / 1 (0.00%) |  |
| occurrences (all)           | 0              | 0             |  |
| Encephalopathy              |                |               |  |
| subjects affected / exposed | 0 / 10 (0.00%) | 0 / 1 (0.00%) |  |
| occurrences (all)           | 0              | 0             |  |
| Hypersomnia                 |                |               |  |
| subjects affected / exposed | 0 / 10 (0.00%) | 0 / 1 (0.00%) |  |
| occurrences (all)           | 0              | 0             |  |
| Hypoaesthesia               |                |               |  |
| subjects affected / exposed | 0 / 10 (0.00%) | 0 / 1 (0.00%) |  |
| occurrences (all)           | 0              | 0             |  |
| Mental impairment           |                |               |  |
| subjects affected / exposed | 0 / 10 (0.00%) | 0 / 1 (0.00%) |  |
| occurrences (all)           | 0              | 0             |  |
| Muscle spasticity           |                |               |  |
| subjects affected / exposed | 0 / 10 (0.00%) | 0 / 1 (0.00%) |  |
| occurrences (all)           | 0              | 0             |  |
| Neurotoxicity               |                |               |  |
| subjects affected / exposed | 0 / 10 (0.00%) | 0 / 1 (0.00%) |  |
| occurrences (all)           | 0              | 0             |  |
| Somnolence                  |                |               |  |
| subjects affected / exposed | 0 / 10 (0.00%) | 0 / 1 (0.00%) |  |
| occurrences (all)           | 0              | 0             |  |
| Syncope                     |                |               |  |

|                                      |                 |                 |  |
|--------------------------------------|-----------------|-----------------|--|
| subjects affected / exposed          | 0 / 10 (0.00%)  | 0 / 1 (0.00%)   |  |
| occurrences (all)                    | 0               | 0               |  |
| Spinal cord compression              |                 |                 |  |
| subjects affected / exposed          | 0 / 10 (0.00%)  | 0 / 1 (0.00%)   |  |
| occurrences (all)                    | 0               | 0               |  |
| Tremor                               |                 |                 |  |
| subjects affected / exposed          | 0 / 10 (0.00%)  | 0 / 1 (0.00%)   |  |
| occurrences (all)                    | 0               | 0               |  |
| Balance disorder                     |                 |                 |  |
| subjects affected / exposed          | 0 / 10 (0.00%)  | 1 / 1 (100.00%) |  |
| occurrences (all)                    | 0               | 1               |  |
| Blood and lymphatic system disorders |                 |                 |  |
| Anaemia                              |                 |                 |  |
| subjects affected / exposed          | 2 / 10 (20.00%) | 0 / 1 (0.00%)   |  |
| occurrences (all)                    | 3               | 0               |  |
| Haemolytic anaemia                   |                 |                 |  |
| subjects affected / exposed          | 0 / 10 (0.00%)  | 0 / 1 (0.00%)   |  |
| occurrences (all)                    | 0               | 0               |  |
| Thrombocytopenia                     |                 |                 |  |
| subjects affected / exposed          | 0 / 10 (0.00%)  | 0 / 1 (0.00%)   |  |
| occurrences (all)                    | 0               | 0               |  |
| Coagulopathy                         |                 |                 |  |
| subjects affected / exposed          | 0 / 10 (0.00%)  | 0 / 1 (0.00%)   |  |
| occurrences (all)                    | 0               | 0               |  |
| Lymphadenopathy                      |                 |                 |  |
| subjects affected / exposed          | 0 / 10 (0.00%)  | 0 / 1 (0.00%)   |  |
| occurrences (all)                    | 0               | 0               |  |
| Microcytic anaemia                   |                 |                 |  |
| subjects affected / exposed          | 0 / 10 (0.00%)  | 0 / 1 (0.00%)   |  |
| occurrences (all)                    | 0               | 0               |  |
| Ear and labyrinth disorders          |                 |                 |  |
| Hypoacusis                           |                 |                 |  |
| subjects affected / exposed          | 0 / 10 (0.00%)  | 0 / 1 (0.00%)   |  |
| occurrences (all)                    | 0               | 0               |  |
| Cerumen impaction                    |                 |                 |  |

|  |                     |                    |  |
|--|---------------------|--------------------|--|
| subjects affected / exposed<br>occurrences (all) | 0 / 10 (0.00%)<br>0 | 0 / 1 (0.00%)<br>0 |  |
| Eye disorders                                    |                     |                    |  |
| Dry eye  |                     |                    |  |
| subjects affected / exposed                      | 1 / 10 (10.00%)     | 0 / 1 (0.00%)      |  |
| occurrences (all)                                | 1                   | 0                  |  |
| Eye disorder                                     |                     |                    |  |
| subjects affected / exposed                      | 0 / 10 (0.00%)      | 0 / 1 (0.00%)      |  |
| occurrences (all)                                | 0                   | 0                  |  |
| Eye pain   |                     |                    |  |
| subjects affected / exposed                      | 0 / 10 (0.00%)      | 0 / 1 (0.00%)      |  |
| occurrences (all)                                | 0                   | 0                  |  |
| Uveitis  |                     |                    |  |
| subjects affected / exposed                      | 1 / 10 (10.00%)     | 0 / 1 (0.00%)      |  |
| occurrences (all)                                | 1                   | 0                  |  |
| Vision blurred                                   |                     |                    |  |
| subjects affected / exposed                      | 2 / 10 (20.00%)     | 0 / 1 (0.00%)      |  |
| occurrences (all)                                | 2                   | 0                  |  |
| Visual impairment                                |                     |                    |  |
| subjects affected / exposed                      | 1 / 10 (10.00%)     | 0 / 1 (0.00%)      |  |
| occurrences (all)                                | 1                   | 0                  |  |
| Eye pruritus                                     |                     |                    |  |
| subjects affected / exposed                      | 0 / 10 (0.00%)      | 0 / 1 (0.00%)      |  |
| occurrences (all)                                | 0                   | 0                  |  |
| Eye swelling                                     |                     |                    |  |
| subjects affected / exposed                      | 0 / 10 (0.00%)      | 0 / 1 (0.00%)      |  |
| occurrences (all)                                | 0                   | 0                  |  |
| Iridocyclitis                                    |                     |                    |  |
| subjects affected / exposed                      | 0 / 10 (0.00%)      | 0 / 1 (0.00%)      |  |
| occurrences (all)                                | 0                   | 0                  |  |
| Lacrimation increased                            |                     |                    |  |
| subjects affected / exposed                      | 0 / 10 (0.00%)      | 0 / 1 (0.00%)      |  |
| occurrences (all)                                | 0                   | 0                  |  |
| Ocular hyperaemia                                |                     |                    |  |
| subjects affected / exposed                      | 0 / 10 (0.00%)      | 0 / 1 (0.00%)      |  |
| occurrences (all)                                | 0                   | 0                  |  |

|  |                      |                      |  |
|--|----------------------|----------------------|--|
| Conjunctival oedema<br>subjects affected / exposed<br>occurrences (all)  | 0 / 10 (0.00%)<br>0  | 1 / 1 (100.00%)<br>2 |  |
| Gastrointestinal disorders   |                      |                      |  |
| Abdominal discomfort<br>subjects affected / exposed<br>occurrences (all) | 0 / 10 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0   |  |
| Abdominal distension<br>subjects affected / exposed<br>occurrences (all) | 0 / 10 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0   |  |
| Abdominal pain<br>subjects affected / exposed<br>occurrences (all)       | 1 / 10 (10.00%)<br>1 | 0 / 1 (0.00%)<br>0   |  |
| Abdominal pain upper<br>subjects affected / exposed<br>occurrences (all) | 0 / 10 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0   |  |
| Anal pruritus<br>subjects affected / exposed<br>occurrences (all)        | 1 / 10 (10.00%)<br>1 | 0 / 1 (0.00%)<br>0   |  |
| Colitis<br>subjects affected / exposed<br>occurrences (all)              | 0 / 10 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0   |  |
| Constipation<br>subjects affected / exposed<br>occurrences (all)         | 2 / 10 (20.00%)<br>3 | 1 / 1 (100.00%)<br>2 |  |
| Diarrhoea<br>subjects affected / exposed<br>occurrences (all)            | 1 / 10 (10.00%)<br>2 | 0 / 1 (0.00%)<br>0   |  |
| Dry mouth<br>subjects affected / exposed<br>occurrences (all)            | 0 / 10 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0   |  |
| Dyspepsia<br>subjects affected / exposed<br>occurrences (all)            | 0 / 10 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0   |  |
| Dysphagia  |                      |                      |  |

|                              |                 |                 |  |
|------------------------------|-----------------|-----------------|--|
| subjects affected / exposed  | 0 / 10 (0.00%)  | 0 / 1 (0.00%)   |  |
| occurrences (all)            | 0               | 0               |  |
| Gastritis                    |                 |                 |  |
| subjects affected / exposed  | 0 / 10 (0.00%)  | 0 / 1 (0.00%)   |  |
| occurrences (all)            | 0               | 0               |  |
| Flatulence                   |                 |                 |  |
| subjects affected / exposed  | 0 / 10 (0.00%)  | 0 / 1 (0.00%)   |  |
| occurrences (all)            | 0               | 0               |  |
| Gastrointestinal haemorrhage |                 |                 |  |
| subjects affected / exposed  | 1 / 10 (10.00%) | 0 / 1 (0.00%)   |  |
| occurrences (all)            | 1               | 0               |  |
| Haemorrhoids                 |                 |                 |  |
| subjects affected / exposed  | 0 / 10 (0.00%)  | 0 / 1 (0.00%)   |  |
| occurrences (all)            | 0               | 0               |  |
| Nausea                       |                 |                 |  |
| subjects affected / exposed  | 2 / 10 (20.00%) | 1 / 1 (100.00%) |  |
| occurrences (all)            | 2               | 2               |  |
| Oral pain                    |                 |                 |  |
| subjects affected / exposed  | 0 / 10 (0.00%)  | 0 / 1 (0.00%)   |  |
| occurrences (all)            | 0               | 0               |  |
| Stomatitis                   |                 |                 |  |
| subjects affected / exposed  | 1 / 10 (10.00%) | 0 / 1 (0.00%)   |  |
| occurrences (all)            | 1               | 0               |  |
| Vomiting                     |                 |                 |  |
| subjects affected / exposed  | 1 / 10 (10.00%) | 1 / 1 (100.00%) |  |
| occurrences (all)            | 1               | 2               |  |
| Abdominal tenderness         |                 |                 |  |
| subjects affected / exposed  | 0 / 10 (0.00%)  | 0 / 1 (0.00%)   |  |
| occurrences (all)            | 0               | 0               |  |
| Aphthous ulcer               |                 |                 |  |
| subjects affected / exposed  | 0 / 10 (0.00%)  | 0 / 1 (0.00%)   |  |
| occurrences (all)            | 0               | 0               |  |
| Autoimmune colitis           |                 |                 |  |
| subjects affected / exposed  | 0 / 10 (0.00%)  | 0 / 1 (0.00%)   |  |
| occurrences (all)            | 0               | 0               |  |
| Ascites                      |                 |                 |  |



|  |                 |               |  |
|--|-----------------|---------------|--|
| subjects affected / exposed            | 0 / 10 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences (all)                      | 0               | 0             |  |
| Chronic gastritis                      |                 |               |  |
| subjects affected / exposed            | 0 / 10 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences (all)                      | 0               | 0             |  |
| Faecaloma                              |                 |               |  |
| subjects affected / exposed            | 0 / 10 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences (all)                      | 0               | 0             |  |
| Gastrooesophageal reflux disease       |                 |               |  |
| subjects affected / exposed            | 0 / 10 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences (all)                      | 0               | 0             |  |
| Hepatobiliary disorders                |                 |               |  |
| Hepatic pain                           |                 |               |  |
| subjects affected / exposed            | 0 / 10 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences (all)                      | 0               | 0             |  |
| Hypertransaminasaemia                  |                 |               |  |
| subjects affected / exposed            | 0 / 10 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences (all)                      | 0               | 0             |  |
| Bile duct obstruction                  |                 |               |  |
| subjects affected / exposed            | 0 / 10 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences (all)                      | 0               | 0             |  |
| Cholelithiasis                         |                 |               |  |
| subjects affected / exposed            | 0 / 10 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences (all)                      | 0               | 0             |  |
| Skin and subcutaneous tissue disorders |                 |               |  |
| Alopecia                               |                 |               |  |
| subjects affected / exposed            | 1 / 10 (10.00%) | 0 / 1 (0.00%) |  |
| occurrences (all)                      | 1               | 0             |  |
| Actinic keratosis                      |                 |               |  |
| subjects affected / exposed            | 0 / 10 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences (all)                      | 0               | 0             |  |
| Dermatitis acneiform                   |                 |               |  |
| subjects affected / exposed            | 0 / 10 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences (all)                      | 0               | 0             |  |
| Dry skin                               |                 |               |  |

|                                    |                 |                 |
|------------------------------------|-----------------|-----------------|
| subjects affected / exposed        | 0 / 10 (0.00%)  | 0 / 1 (0.00%)   |
| occurrences (all)                  | 0               | 0               |
| Dermatitis exfoliative generalised |                 |                 |
| subjects affected / exposed        | 0 / 10 (0.00%)  | 0 / 1 (0.00%)   |
| occurrences (all)                  | 0               | 0               |
| Hyperhidrosis                      |                 |                 |
| subjects affected / exposed        | 0 / 10 (0.00%)  | 1 / 1 (100.00%) |
| occurrences (all)                  | 0               | 1               |
| Eczema nummular                    |                 |                 |
| subjects affected / exposed        | 1 / 10 (10.00%) | 0 / 1 (0.00%)   |
| occurrences (all)                  | 1               | 0               |
| Lichenoid keratosis                |                 |                 |
| subjects affected / exposed        | 1 / 10 (10.00%) | 0 / 1 (0.00%)   |
| occurrences (all)                  | 1               | 0               |
| Livedo reticularis                 |                 |                 |
| subjects affected / exposed        | 0 / 10 (0.00%)  | 0 / 1 (0.00%)   |
| occurrences (all)                  | 0               | 0               |
| Pruritus                           |                 |                 |
| subjects affected / exposed        | 6 / 10 (60.00%) | 1 / 1 (100.00%) |
| occurrences (all)                  | 6               | 1               |
| Rash                               |                 |                 |
| subjects affected / exposed        | 3 / 10 (30.00%) | 0 / 1 (0.00%)   |
| occurrences (all)                  | 3               | 0               |
| Rash erythematous                  |                 |                 |
| subjects affected / exposed        | 0 / 10 (0.00%)  | 0 / 1 (0.00%)   |
| occurrences (all)                  | 0               | 0               |
| Rash maculo-papular                |                 |                 |
| subjects affected / exposed        | 1 / 10 (10.00%) | 0 / 1 (0.00%)   |
| occurrences (all)                  | 1               | 0               |
| Rash papular                       |                 |                 |
| subjects affected / exposed        | 0 / 10 (0.00%)  | 0 / 1 (0.00%)   |
| occurrences (all)                  | 0               | 0               |
| Rash pruritic                      |                 |                 |
| subjects affected / exposed        | 0 / 10 (0.00%)  | 0 / 1 (0.00%)   |
| occurrences (all)                  | 0               | 0               |
| Scab                               |                 |                 |

|                             |                 |                 |  |
|-----------------------------|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 10 (0.00%)  | 0 / 1 (0.00%)   |  |
| occurrences (all)           | 0               | 0               |  |
| Skin hypopigmentation       |                 |                 |  |
| subjects affected / exposed | 2 / 10 (20.00%) | 0 / 1 (0.00%)   |  |
| occurrences (all)           | 2               | 0               |  |
| Vitiligo                    |                 |                 |  |
| subjects affected / exposed | 0 / 10 (0.00%)  | 0 / 1 (0.00%)   |  |
| occurrences (all)           | 0               | 0               |  |
| Erythema                    |                 |                 |  |
| subjects affected / exposed | 0 / 10 (0.00%)  | 0 / 1 (0.00%)   |  |
| occurrences (all)           | 0               | 0               |  |
| Night sweats                |                 |                 |  |
| subjects affected / exposed | 0 / 10 (0.00%)  | 0 / 1 (0.00%)   |  |
| occurrences (all)           | 0               | 0               |  |
| Scar pain                   |                 |                 |  |
| subjects affected / exposed | 0 / 10 (0.00%)  | 0 / 1 (0.00%)   |  |
| occurrences (all)           | 0               | 0               |  |
| Skin ulcer                  |                 |                 |  |
| subjects affected / exposed | 0 / 10 (0.00%)  | 0 / 1 (0.00%)   |  |
| occurrences (all)           | 0               | 0               |  |
| Facial wasting              |                 |                 |  |
| subjects affected / exposed | 0 / 10 (0.00%)  | 1 / 1 (100.00%) |  |
| occurrences (all)           | 0               | 1               |  |
| Renal and urinary disorders |                 |                 |  |
| Chromaturia                 |                 |                 |  |
| subjects affected / exposed | 1 / 10 (10.00%) | 0 / 1 (0.00%)   |  |
| occurrences (all)           | 1               | 0               |  |
| Acute kidney injury         |                 |                 |  |
| subjects affected / exposed | 0 / 10 (0.00%)  | 0 / 1 (0.00%)   |  |
| occurrences (all)           | 0               | 0               |  |
| Dysuria                     |                 |                 |  |
| subjects affected / exposed | 0 / 10 (0.00%)  | 0 / 1 (0.00%)   |  |
| occurrences (all)           | 0               | 0               |  |
| Pollakiuria                 |                 |                 |  |
| subjects affected / exposed | 1 / 10 (10.00%) | 0 / 1 (0.00%)   |  |
| occurrences (all)           | 1               | 0               |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| Haematuria                                      |                 |                 |  |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 0 / 1 (0.00%)   |  |
| occurrences (all)                               | 0               | 0               |  |
| Nocturia  |                 |                 |  |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 0 / 1 (0.00%)   |  |
| occurrences (all)                               | 0               | 0               |  |
| Polyuria  |                 |                 |  |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 0 / 1 (0.00%)   |  |
| occurrences (all)                               | 0               | 0               |  |
| Urinary hesitation                              |                 |                 |  |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 0 / 1 (0.00%)   |  |
| occurrences (all)                               | 0               | 0               |  |
| Urinary incontinence                            |                 |                 |  |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 0 / 1 (0.00%)   |  |
| occurrences (all)                               | 0               | 0               |  |
| Endocrine disorders                             |                 |                 |  |
| Adrenal insufficiency                           |                 |                 |  |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 0 / 1 (0.00%)   |  |
| occurrences (all)                               | 0               | 0               |  |
| Endocrine disorder                              |                 |                 |  |
| subjects affected / exposed                     | 1 / 10 (10.00%) | 0 / 1 (0.00%)   |  |
| occurrences (all)                               | 2               | 0               |  |
| Hyperthyroidism                                 |                 |                 |  |
| subjects affected / exposed                     | 1 / 10 (10.00%) | 0 / 1 (0.00%)   |  |
| occurrences (all)                               | 1               | 0               |  |
| Hypophysitis                                    |                 |                 |  |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 0 / 1 (0.00%)   |  |
| occurrences (all)                               | 0               | 0               |  |
| Hypothyroidism                                  |                 |                 |  |
| subjects affected / exposed                     | 1 / 10 (10.00%) | 1 / 1 (100.00%) |  |
| occurrences (all)                               | 1               | 1               |  |
| Thyroiditis                                     |                 |                 |  |
| subjects affected / exposed                     | 0 / 10 (0.00%)  | 0 / 1 (0.00%)   |  |
| occurrences (all)                               | 0               | 0               |  |
| Musculoskeletal and connective tissue disorders |                 |                 |  |

|                                 |                 |                 |
|---------------------------------|-----------------|-----------------|
| Arthralgia                      |                 |                 |
| subjects affected / exposed     | 2 / 10 (20.00%) | 0 / 1 (0.00%)   |
| occurrences (all)               | 3               | 0               |
| Arthritis                       |                 |                 |
| subjects affected / exposed     | 0 / 10 (0.00%)  | 0 / 1 (0.00%)   |
| occurrences (all)               | 0               | 0               |
| Back pain                       |                 |                 |
| subjects affected / exposed     | 2 / 10 (20.00%) | 0 / 1 (0.00%)   |
| occurrences (all)               | 3               | 0               |
| Bone pain                       |                 |                 |
| subjects affected / exposed     | 0 / 10 (0.00%)  | 0 / 1 (0.00%)   |
| occurrences (all)               | 0               | 0               |
| Flank pain                      |                 |                 |
| subjects affected / exposed     | 0 / 10 (0.00%)  | 1 / 1 (100.00%) |
| occurrences (all)               | 0               | 1               |
| Joint range of motion decreased |                 |                 |
| subjects affected / exposed     | 0 / 10 (0.00%)  | 0 / 1 (0.00%)   |
| occurrences (all)               | 0               | 0               |
| Muscle spasms                   |                 |                 |
| subjects affected / exposed     | 1 / 10 (10.00%) | 0 / 1 (0.00%)   |
| occurrences (all)               | 1               | 0               |
| Musculoskeletal pain            |                 |                 |
| subjects affected / exposed     | 1 / 10 (10.00%) | 0 / 1 (0.00%)   |
| occurrences (all)               | 2               | 0               |
| Muscular weakness               |                 |                 |
| subjects affected / exposed     | 0 / 10 (0.00%)  | 0 / 1 (0.00%)   |
| occurrences (all)               | 0               | 0               |
| Neck pain                       |                 |                 |
| subjects affected / exposed     | 1 / 10 (10.00%) | 0 / 1 (0.00%)   |
| occurrences (all)               | 1               | 0               |
| Myalgia                         |                 |                 |
| subjects affected / exposed     | 1 / 10 (10.00%) | 0 / 1 (0.00%)   |
| occurrences (all)               | 1               | 0               |
| Pain in extremity               |                 |                 |
| subjects affected / exposed     | 1 / 10 (10.00%) | 0 / 1 (0.00%)   |
| occurrences (all)               | 2               | 0               |

|                             |                 |                 |  |
|-----------------------------|-----------------|-----------------|--|
| Pain in jaw                 |                 |                 |  |
| subjects affected / exposed | 0 / 10 (0.00%)  | 0 / 1 (0.00%)   |  |
| occurrences (all)           | 0               | 0               |  |
| Musculoskeletal stiffness   |                 |                 |  |
| subjects affected / exposed | 0 / 10 (0.00%)  | 0 / 1 (0.00%)   |  |
| occurrences (all)           | 0               | 0               |  |
| Infections and infestations |                 |                 |  |
| Candida infection           |                 |                 |  |
| subjects affected / exposed | 0 / 10 (0.00%)  | 0 / 1 (0.00%)   |  |
| occurrences (all)           | 0               | 0               |  |
| Cellulitis                  |                 |                 |  |
| subjects affected / exposed | 0 / 10 (0.00%)  | 0 / 1 (0.00%)   |  |
| occurrences (all)           | 0               | 0               |  |
| Conjunctivitis              |                 |                 |  |
| subjects affected / exposed | 0 / 10 (0.00%)  | 0 / 1 (0.00%)   |  |
| occurrences (all)           | 0               | 0               |  |
| Influenza                   |                 |                 |  |
| subjects affected / exposed | 0 / 10 (0.00%)  | 0 / 1 (0.00%)   |  |
| occurrences (all)           | 0               | 0               |  |
| Cytomegalovirus infection   |                 |                 |  |
| subjects affected / exposed | 0 / 10 (0.00%)  | 0 / 1 (0.00%)   |  |
| occurrences (all)           | 0               | 0               |  |
| Pneumonia                   |                 |                 |  |
| subjects affected / exposed | 0 / 10 (0.00%)  | 0 / 1 (0.00%)   |  |
| occurrences (all)           | 0               | 0               |  |
| Nasopharyngitis             |                 |                 |  |
| subjects affected / exposed | 1 / 10 (10.00%) | 1 / 1 (100.00%) |  |
| occurrences (all)           | 1               | 1               |  |
| Rash pustular               |                 |                 |  |
| subjects affected / exposed | 0 / 10 (0.00%)  | 0 / 1 (0.00%)   |  |
| occurrences (all)           | 0               | 0               |  |
| Respiratory tract infection |                 |                 |  |
| subjects affected / exposed | 0 / 10 (0.00%)  | 0 / 1 (0.00%)   |  |
| occurrences (all)           | 0               | 0               |  |
| Rhinitis                    |                 |                 |  |

|                                   |                 |               |  |
|-----------------------------------|-----------------|---------------|--|
| subjects affected / exposed       | 0 / 10 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences (all)                 | 0               | 0             |  |
| Sepsis                            |                 |               |  |
| subjects affected / exposed       | 0 / 10 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences (all)                 | 0               | 0             |  |
| Sinusitis                         |                 |               |  |
| subjects affected / exposed       | 0 / 10 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences (all)                 | 0               | 0             |  |
| Skin infection                    |                 |               |  |
| subjects affected / exposed       | 0 / 10 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences (all)                 | 0               | 0             |  |
| Upper respiratory tract infection |                 |               |  |
| subjects affected / exposed       | 1 / 10 (10.00%) | 0 / 1 (0.00%) |  |
| occurrences (all)                 | 1               | 0             |  |
| Urinary tract infection           |                 |               |  |
| subjects affected / exposed       | 0 / 10 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences (all)                 | 0               | 0             |  |
| Fungal skin infection             |                 |               |  |
| subjects affected / exposed       | 0 / 10 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences (all)                 | 0               | 0             |  |
| Hordeolum                         |                 |               |  |
| subjects affected / exposed       | 0 / 10 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences (all)                 | 0               | 0             |  |
| Infected skin ulcer               |                 |               |  |
| subjects affected / exposed       | 0 / 10 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences (all)                 | 0               | 0             |  |
| Laryngitis                        |                 |               |  |
| subjects affected / exposed       | 0 / 10 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences (all)                 | 0               | 0             |  |
| Onychomycosis                     |                 |               |  |
| subjects affected / exposed       | 0 / 10 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences (all)                 | 0               | 0             |  |
| Oral candidiasis                  |                 |               |  |
| subjects affected / exposed       | 0 / 10 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences (all)                 | 0               | 0             |  |
| Oral herpes                       |                 |               |  |

|                                    |                 |                 |  |
|------------------------------------|-----------------|-----------------|--|
| subjects affected / exposed        | 0 / 10 (0.00%)  | 0 / 1 (0.00%)   |  |
| occurrences (all)                  | 0               | 0               |  |
| Pyuria                             |                 |                 |  |
| subjects affected / exposed        | 0 / 10 (0.00%)  | 0 / 1 (0.00%)   |  |
| occurrences (all)                  | 0               | 0               |  |
| Staphylococcal infection           |                 |                 |  |
| subjects affected / exposed        | 0 / 10 (0.00%)  | 0 / 1 (0.00%)   |  |
| occurrences (all)                  | 0               | 0               |  |
| Herpes zoster                      |                 |                 |  |
| subjects affected / exposed        | 0 / 10 (0.00%)  | 1 / 1 (100.00%) |  |
| occurrences (all)                  | 0               | 1               |  |
| Metabolism and nutrition disorders |                 |                 |  |
| Decreased appetite                 |                 |                 |  |
| subjects affected / exposed        | 1 / 10 (10.00%) | 1 / 1 (100.00%) |  |
| occurrences (all)                  | 2               | 1               |  |
| Dehydration                        |                 |                 |  |
| subjects affected / exposed        | 1 / 10 (10.00%) | 1 / 1 (100.00%) |  |
| occurrences (all)                  | 2               | 3               |  |
| Hypercalcaemia                     |                 |                 |  |
| subjects affected / exposed        | 1 / 10 (10.00%) | 0 / 1 (0.00%)   |  |
| occurrences (all)                  | 1               | 0               |  |
| Hyperglycaemia                     |                 |                 |  |
| subjects affected / exposed        | 2 / 10 (20.00%) | 0 / 1 (0.00%)   |  |
| occurrences (all)                  | 8               | 0               |  |
| Hyperuricaemia                     |                 |                 |  |
| subjects affected / exposed        | 0 / 10 (0.00%)  | 0 / 1 (0.00%)   |  |
| occurrences (all)                  | 0               | 0               |  |
| Hypoalbuminaemia                   |                 |                 |  |
| subjects affected / exposed        | 1 / 10 (10.00%) | 0 / 1 (0.00%)   |  |
| occurrences (all)                  | 1               | 0               |  |
| Hypoglycaemia                      |                 |                 |  |
| subjects affected / exposed        | 2 / 10 (20.00%) | 0 / 1 (0.00%)   |  |
| occurrences (all)                  | 2               | 0               |  |
| Hypokalaemia                       |                 |                 |  |
| subjects affected / exposed        | 0 / 10 (0.00%)  | 0 / 1 (0.00%)   |  |
| occurrences (all)                  | 0               | 0               |  |



|                             |                 |               |  |
|-----------------------------|-----------------|---------------|--|
| Hypomagnesaemia             |                 |               |  |
| subjects affected / exposed | 1 / 10 (10.00%) | 0 / 1 (0.00%) |  |
| occurrences (all)           | 1               | 0             |  |
| Hyponatraemia               |                 |               |  |
| subjects affected / exposed | 1 / 10 (10.00%) | 0 / 1 (0.00%) |  |
| occurrences (all)           | 1               | 0             |  |
| Hypophosphataemia           |                 |               |  |
| subjects affected / exposed | 1 / 10 (10.00%) | 0 / 1 (0.00%) |  |
| occurrences (all)           | 1               | 0             |  |
| Lactic acidosis             |                 |               |  |
| subjects affected / exposed | 0 / 10 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences (all)           | 0               | 0             |  |
| Malnutrition                |                 |               |  |
| subjects affected / exposed | 0 / 10 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences (all)           | 0               | 0             |  |
| Diabetes mellitus           |                 |               |  |
| subjects affected / exposed | 0 / 10 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences (all)           | 0               | 0             |  |
| Fluid retention             |                 |               |  |
| subjects affected / exposed | 0 / 10 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences (all)           | 0               | 0             |  |
| Hyperkalaemia               |                 |               |  |
| subjects affected / exposed | 0 / 10 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences (all)           | 0               | 0             |  |
| Hypocalcaemia               |                 |               |  |
| subjects affected / exposed | 0 / 10 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences (all)           | 0               | 0             |  |
| Hypophagia                  |                 |               |  |
| subjects affected / exposed | 0 / 10 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences (all)           | 0               | 0             |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported