



## Clinical trial results:

### A Phase 2b Randomized Study to Assess the Efficacy and Safety of the Combination of Ublituximab + Umbralisib With or Without Bendamustine and Umbralisib Alone in Patients With Previously Treated Non-Hodgkin's Lymphoma

#### Summary

|                          |                |
|--------------------------|----------------|
| EudraCT number           | 2016-004718-90 |
| Trial protocol           | GB PL SK ES IT |
| Global end of trial date | 04 July 2022   |

#### Results information

|                                |              |
|--------------------------------|--------------|
| Result version number          | v1 (current) |
| This version publication date  | 19 July 2023 |
| First version publication date | 19 July 2023 |

#### Trial information

##### Trial identification

|                       |             |
|-----------------------|-------------|
| Sponsor protocol code | UTX-TGR-205 |
|-----------------------|-------------|

##### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT02793583 |
| WHO universal trial number (UTN)   | -           |

Notes:

#### Sponsors

|                              |                                                                                        |
|------------------------------|----------------------------------------------------------------------------------------|
| Sponsor organisation name    | TG Therapeutics, Inc                                                                   |
| Sponsor organisation address | 2 Gansevoort St., 9th Floor, New York, NY 10014, United States,                        |
| Public contact               | Izabela Kozdraś-Urbaneck, Brilliance Sp. z o.o., +48 668166876, ikozdras@brilliance.pl |
| Scientific contact           | Izabela Kozdraś-Urbaneck, Brilliance Sp. z o.o., +48 668166876, ikozdras@brilliance.pl |

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                       | 04 July 2022 |
| Is this the analysis of the primary completion data? | No           |
| Global end of trial reached?                         | Yes          |
| Global end of trial date                             | 04 July 2022 |
| Was the trial ended prematurely?                     | Yes          |

Notes:

## General information about the trial

Main objective of the trial:

Unity NHL - A Phase 2b randomised study to assess the efficacy and safety of the combination of ublituximab + umbralisib with or without bendamustine and umbralisib alone in subjects with previously treated non-hodgkin's lymphoma.

The purpose of this study was to evaluate the efficacy and safety of umbralisib monotherapy and the umbralisib + ublituximab (U2) combination in aggressive and indolent lymphomas and to also explore the U2 regimen in combination with bendamustine in the treatment of non-Hodgkin lymphomas (NHL) (follicular lymphoma (FL), small lymphocytic lymphoma (SLL), marginal zone lymphoma (MZL), diffuse large B-cell lymphoma (DLBCL) and mantle cell lymphoma (MCL).

Protection of trial subjects:

All study subjects were required to read and sign an informed consent form.

Background therapy: -

Evidence for comparator: -

|                                                           |             |
|-----------------------------------------------------------|-------------|
| Actual start date of recruitment                          | 25 May 2016 |
| Long term follow-up planned                               | No          |
| Independent data monitoring committee (IDMC) involvement? | Yes         |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |                        |
|--------------------------------------|------------------------|
| Country: Number of subjects enrolled | Slovakia: 10           |
| Country: Number of subjects enrolled | Spain: 15              |
| Country: Number of subjects enrolled | United Kingdom: 45     |
| Country: Number of subjects enrolled | Italy: 43              |
| Country: Number of subjects enrolled | Australia: 29          |
| Country: Number of subjects enrolled | Israel: 34             |
| Country: Number of subjects enrolled | Poland: 94             |
| Country: Number of subjects enrolled | United States: 449     |
| Country: Number of subjects enrolled | Korea, Republic of: 16 |
| Worldwide total number of subjects   | 735                    |
| EEA total number of subjects         | 162                    |

Notes:

| <b>Subjects enrolled per age group</b>    |     |
|-------------------------------------------|-----|
| In utero                                  | 0   |
| Preterm newborn - gestational age < 37 wk | 0   |
| Newborns (0-27 days)                      | 0   |
| Infants and toddlers (28 days-23 months)  | 0   |
| Children (2-11 years)                     | 0   |
| Adolescents (12-17 years)                 | 0   |
| Adults (18-64 years)                      | 277 |
| From 65 to 84 years                       | 418 |
| 85 years and over                         | 40  |

## Subject disposition

### Recruitment

Recruitment details:

A total of 735 subjects took part in the study at 141 investigative sites in Australia, Israel, Italy, Poland, Slovakia, South Korea, Spain, the United Kingdom, and the United States from 25 May 2016 to 4 July 2022.

### Pre-assignment

Screening details:

After screening, a total of 735 subjects were enrolled in the study.

### 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>             | Arm A: Ublituximab + Umbralisib (TGR-1202) |

Arm description:

Subjects with FL, MZL, MCL, and DLBCL received ublituximab, 900 milligrams (mg), intravenous (IV), infusion on Days 1, 8, and 15 of Cycle 1, Day 1 of Cycles 2-6, and thereafter on Day 1 of every 3 cycles, through Cycle 24 (1 cycle=28 days) in combination with umbralisib, 800 mg, orally, once daily, through Cycles 1-24 or until disease progression, unacceptable toxicity or withdrawal from the study for other reasons.

|                                        |                 |
|----------------------------------------|-----------------|
| Arm type                               | Experimental    |
| Investigational medicinal product name | Ublituximab     |
| Investigational medicinal product code |                 |
| Other name                             | TG-1101         |
| Pharmaceutical forms                   | Infusion        |
| Routes of administration               | Intravenous use |

Dosage and administration details:

Ublituximab, 900 mg, was administered as IV infusion

|                                        |            |
|----------------------------------------|------------|
| Investigational medicinal product name | Umbralisib |
| Investigational medicinal product code |            |
| Other name                             | TGR-1202   |
| Pharmaceutical forms                   | Tablet     |
| Routes of administration               | Oral use   |

Dosage and administration details:

Umbralisib, 800 mg, tablet was administered orally

|                  |                                          |
|------------------|------------------------------------------|
| <b>Arm title</b> | Arm B: Umbralisib (TGR-1202) Monotherapy |
|------------------|------------------------------------------|

Arm description:

Subjects with FL, SLL, MZL, MCL, and DLBCL received umbralisib 800 mg orally, once daily through Cycles 1-24 (1 cycle=28 days), or until disease progression, unacceptable toxicity, or withdrawal from the study for other reasons.

|                                        |              |
|----------------------------------------|--------------|
| Arm type                               | Experimental |
| Investigational medicinal product name | Umbralisib   |
| Investigational medicinal product code |              |
| Other name                             | TGR-1202     |
| Pharmaceutical forms                   | Tablet       |
| Routes of administration               | Oral use     |

**Dosage and administration details:**

Umbralisib, 800 mg, tablet was administered orally

|                  |                                                           |
|------------------|-----------------------------------------------------------|
| <b>Arm title</b> | Arm C: Ublituximab + Umbralisib (TGR-1202) + Bendamustine |
|------------------|-----------------------------------------------------------|

**Arm description:**

Subjects with DLBCL received ublituximab 900 mg, IV infusion, on Days 1, 8, and 15 of Cycle 1, Day 1 of Cycles 2-6 and, thereafter on Day 1 of every 3 cycles, through Cycle 24 (1 cycle=28 days) in combination with umbralisib, 800 mg orally, once daily through Cycles 1-24 and bendamustine 90 milligrams per square meter (mg/m<sup>2</sup>), IV infusion, on Days 1 and 2 of Cycles 1-6 or until disease progression, unacceptable toxicity or withdrawal from the study for other reasons.

|                                        |                 |
|----------------------------------------|-----------------|
| Arm type                               | Experimental    |
| Investigational medicinal product name | Ublituximab     |
| Investigational medicinal product code |                 |
| Other name                             | TG-1101         |
| Pharmaceutical forms                   | Infusion        |
| Routes of administration               | Intravenous use |

**Dosage and administration details:**

Ublituximab, 900 mg, was administered as IV infusion

|                                        |            |
|----------------------------------------|------------|
| Investigational medicinal product name | Umbralisib |
| Investigational medicinal product code |            |
| Other name                             | TGR-1202   |
| Pharmaceutical forms                   | Tablet     |
| Routes of administration               | Oral use   |

**Dosage and administration details:**

Umbralisib, 800 mg, tablet was administered orally

|                                        |                 |
|----------------------------------------|-----------------|
| Investigational medicinal product name | Bendamustine    |
| Investigational medicinal product code |                 |
| Other name                             | Treanda         |
| Pharmaceutical forms                   | Infusion        |
| Routes of administration               | Intravenous use |

**Dosage and administration details:**

Bendamustine, 100 mg, was administered as IV infusion

|                  |                                |
|------------------|--------------------------------|
| <b>Arm title</b> | Arm D: Ublituximab Monotherapy |
|------------------|--------------------------------|

**Arm description:**

Subjects with FL received ublituximab 900 mg, IV infusion, on Days 1, 8, and 15 of Cycle 1, Day 1 of Cycles 2-6 and, thereafter on Day 1 of every 3 cycles, through Cycle 24 (1 cycle=28 days) or until disease progression, unacceptable toxicity, or withdrawal from the study for other reasons.

|                                        |                 |
|----------------------------------------|-----------------|
| Arm type                               | Experimental    |
| Investigational medicinal product name | Ublituximab     |
| Investigational medicinal product code |                 |
| Other name                             | TG-1101         |
| Pharmaceutical forms                   | Infusion        |
| Routes of administration               | Intravenous use |

**Dosage and administration details:**

Ublituximab, 900 mg, was administered as IV infusion

|                  |                                             |
|------------------|---------------------------------------------|
| <b>Arm title</b> | Arm E: Ublituximab to Umbralisib (TGR-1202) |
|------------------|---------------------------------------------|

**Arm description:**

Subjects in Arm D were crossed over to umbralisib monotherapy upon confirmation of progressive disease (PD) by the independent review committee (IRC) to receive umbralisib, 800 mg orally, once daily, through Cycles 1-24 (1 cycle=28 days) or until disease progression, unacceptable toxicity, or withdrawal from the study for other reasons.

|                                        |              |
|----------------------------------------|--------------|
| Arm type                               | Experimental |
| Investigational medicinal product name | Umbralisib   |
| Investigational medicinal product code |              |
| Other name                             | TGR-1202     |
| Pharmaceutical forms                   | Tablet       |
| Routes of administration               | Oral use     |

Dosage and administration details:

Umbralisib, 800 mg, tablet was administered orally

| Number of subjects in period 1                 | Arm A: Ublituximab + Umbralisib (TGR-1202) | Arm B: Umbralisib (TGR-1202) Monotherapy | Arm C: Ublituximab + Umbralisib (TGR-1202) + Bendamustine |
|------------------------------------------------|--------------------------------------------|------------------------------------------|-----------------------------------------------------------|
|                                                |                                            |                                          |                                                           |
| Started                                        | 262                                        | 307                                      | 130                                                       |
| Completed                                      | 0                                          | 0                                        | 0                                                         |
| Not completed                                  | 262                                        | 307                                      | 130                                                       |
| Adverse Event                                  | 5                                          | 13                                       | 7                                                         |
| Completion of Protocol Specified Regimen       | 1                                          | -                                        | 1                                                         |
| Investigator Decision                          | 22                                         | 32                                       | 10                                                        |
| Study Terminated by Sponsor                    | 56                                         | 32                                       | 7                                                         |
| Withdrawal of Consent                          | 15                                         | 19                                       | 12                                                        |
| Unknown/Missing                                | 1                                          | 1                                        | -                                                         |
| Non-compliance with Study                      | 1                                          | 1                                        | 2                                                         |
| Death                                          | 34                                         | 18                                       | 13                                                        |
| Progressive Disease                            | 108                                        | 173                                      | 73                                                        |
| Lost to follow-up                              | 1                                          | -                                        | 1                                                         |
| Reason not Specified                           | 6                                          | 4                                        | 3                                                         |
| Initiation of Non-protocol Anti-cancer Therapy | 10                                         | 8                                        | 1                                                         |
| Lack of efficacy                               | 2                                          | 6                                        | -                                                         |

| Number of subjects in period 1           | Arm D: Ublituximab Monotherapy | Arm E: Ublituximab to Umbralisib (TGR-1202) |
|------------------------------------------|--------------------------------|---------------------------------------------|
|                                          |                                |                                             |
| Started                                  | 24                             | 12                                          |
| Completed                                | 0                              | 0                                           |
| Not completed                            | 24                             | 12                                          |
| Adverse Event                            | -                              | -                                           |
| Completion of Protocol Specified Regimen | -                              | -                                           |
| Investigator Decision                    | 2                              | 5                                           |
| Study Terminated by Sponsor              | 1                              | 1                                           |
| Withdrawal of Consent                    | 2                              | -                                           |
| Unknown/Missing                          | -                              | -                                           |

|                                                |    |   |
|------------------------------------------------|----|---|
| Non-compliance with Study                      | -  | - |
| Death                                          | 2  | 1 |
| Progressive Disease                            | 17 | 4 |
| Lost to follow-up                              | -  | - |
| Reason not Specified                           | -  | - |
| Initiation of Non-protocol Anti-cancer Therapy | -  | 1 |
| Lack of efficacy                               | -  | - |

## Baseline characteristics

### Reporting groups

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                                                           |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------|
| Reporting group title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | Arm A: Ublituximab + Umbralisib (TGR-1202)                |
| Reporting group description:<br>Subjects with FL, MZL, MCL, and DLBCL received ublituximab, 900 milligrams (mg), intravenous (IV), infusion on Days 1, 8, and 15 of Cycle 1, Day 1 of Cycles 2-6, and thereafter on Day 1 of every 3 cycles, through Cycle 24 (1 cycle=28 days) in combination with umbralisib, 800 mg, orally, once daily, through Cycles 1-24 or until disease progression, unacceptable toxicity or withdrawal from the study for other reasons.                                                                  |                                                           |
| Reporting group title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | Arm B: Umbralisib (TGR-1202) Monotherapy                  |
| Reporting group description:<br>Subjects with FL, SLL, MZL, MCL, and DLBCL received umbralisib 800 mg orally, once daily through Cycles 1-24 (1 cycle=28 days), or until disease progression, unacceptable toxicity, or withdrawal from the study for other reasons.                                                                                                                                                                                                                                                                 |                                                           |
| Reporting group title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | Arm C: Ublituximab + Umbralisib (TGR-1202) + Bendamustine |
| Reporting group description:<br>Subjects with DLBCL received ublituximab 900 mg, IV infusion, on Days 1, 8, and 15 of Cycle 1, Day 1 of Cycles 2-6 and, thereafter on Day 1 of every 3 cycles, through Cycle 24 (1 cycle=28 days) in combination with umbralisib, 800 mg orally, once daily through Cycles 1-24 and bendamustine 90 milligrams per square meter (mg/m <sup>2</sup> ), IV infusion, on Days 1 and 2 of Cycles 1-6 or until disease progression, unacceptable toxicity or withdrawal from the study for other reasons. |                                                           |
| Reporting group title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | Arm D: Ublituximab Monotherapy                            |
| Reporting group description:<br>Subjects with FL received ublituximab 900 mg, IV infusion, on Days 1, 8, and 15 of Cycle 1, Day 1 of Cycles 2-6 and, thereafter on Day 1 of every 3 cycles, through Cycle 24 (1 cycle=28 days) or until disease progression, unacceptable toxicity, or withdrawal from the study for other reasons.                                                                                                                                                                                                  |                                                           |
| Reporting group title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | Arm E: Ublituximab to Umbralisib (TGR-1202)               |
| Reporting group description:<br>Subjects in Arm D were crossed over to umbralisib monotherapy upon confirmation of progressive disease (PD) by the independent review committee (IRC) to receive umbralisib, 800 mg orally, once daily, through Cycles 1-24 (1 cycle=28 days) or until disease progression, unacceptable toxicity, or withdrawal from the study for other reasons.                                                                                                                                                   |                                                           |

| Reporting group values                | Arm A: Ublituximab + Umbralisib (TGR-1202) | Arm B: Umbralisib (TGR-1202) Monotherapy | Arm C: Ublituximab + Umbralisib (TGR-1202) + Bendamustine |
|---------------------------------------|--------------------------------------------|------------------------------------------|-----------------------------------------------------------|
| Number of subjects                    | 262                                        | 307                                      | 130                                                       |
| Age categorical<br>Units: Subjects    |                                            |                                          |                                                           |
| Adults (18-64 years)                  | 87                                         | 131                                      | 40                                                        |
| From 65-84 years                      | 158                                        | 164                                      | 79                                                        |
| 85 years and over                     | 17                                         | 12                                       | 11                                                        |
| Age continuous<br>Units: years        |                                            |                                          |                                                           |
| arithmetic mean                       | 68.4                                       | 66.0                                     | 69.6                                                      |
| standard deviation                    | ± 11.15                                    | ± 11.13                                  | ± 11.25                                                   |
| Gender categorical<br>Units: Subjects |                                            |                                          |                                                           |
| Female                                | 105                                        | 139                                      | 52                                                        |
| Male                                  | 157                                        | 168                                      | 78                                                        |

|                                           |     |     |     |
|-------------------------------------------|-----|-----|-----|
| Race                                      |     |     |     |
| Units: Subjects                           |     |     |     |
| White                                     | 211 | 256 | 114 |
| Black or African American                 | 8   | 12  | 5   |
| Asian                                     | 12  | 10  | 4   |
| American Indian or Alaska Native          | 0   | 2   | 0   |
| Native Hawaiian or Other Pacific Islander | 0   | 2   | 0   |
| Multiple                                  | 2   | 0   | 0   |
| Other                                     | 3   | 5   | 0   |
| Not Reported                              | 26  | 20  | 7   |
| Ethnicity                                 |     |     |     |
| Units: Subjects                           |     |     |     |
| Hispanic or Latino                        | 18  | 15  | 2   |
| Not Hispanic or Latino                    | 210 | 268 | 115 |
| Not Reported                              | 34  | 24  | 13  |

| Reporting group values                    | Arm D: Ublituximab Monotherapy | Arm E: Ublituximab to Umbralisib (TGR-1202) | Total |
|-------------------------------------------|--------------------------------|---------------------------------------------|-------|
| Number of subjects                        | 24                             | 12                                          | 735   |
| Age categorical                           |                                |                                             |       |
| Units: Subjects                           |                                |                                             |       |
| Adults (18-64 years)                      | 13                             | 6                                           | 277   |
| From 65-84 years                          | 11                             | 6                                           | 418   |
| 85 years and over                         | 0                              | 0                                           | 40    |
| Age continuous                            |                                |                                             |       |
| Units: years                              |                                |                                             |       |
| arithmetic mean                           | 62.9                           | 62.8                                        |       |
| standard deviation                        | ± 10.63                        | ± 10.26                                     | -     |
| Gender categorical                        |                                |                                             |       |
| Units: Subjects                           |                                |                                             |       |
| Female                                    | 8                              | 4                                           | 308   |
| Male                                      | 16                             | 8                                           | 427   |
| Race                                      |                                |                                             |       |
| Units: Subjects                           |                                |                                             |       |
| White                                     | 19                             | 9                                           | 609   |
| Black or African American                 | 1                              | 1                                           | 27    |
| Asian                                     | 0                              | 0                                           | 26    |
| American Indian or Alaska Native          | 0                              | 0                                           | 2     |
| Native Hawaiian or Other Pacific Islander | 0                              | 0                                           | 2     |
| Multiple                                  | 0                              | 0                                           | 2     |
| Other                                     | 0                              | 0                                           | 8     |
| Not Reported                              | 4                              | 2                                           | 59    |
| Ethnicity                                 |                                |                                             |       |
| Units: Subjects                           |                                |                                             |       |
| Hispanic or Latino                        | 2                              | 1                                           | 38    |
| Not Hispanic or Latino                    | 19                             | 11                                          | 623   |
| Not Reported                              | 3                              | 0                                           | 74    |

## End points

### End points reporting groups

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                                                           |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------|
| Reporting group title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | Arm A: Ublituximab + Umbralisib (TGR-1202)                |
| Reporting group description:<br>Subjects with FL, MZL, MCL, and DLBCL received ublituximab, 900 milligrams (mg), intravenous (IV), infusion on Days 1, 8, and 15 of Cycle 1, Day 1 of Cycles 2-6, and thereafter on Day 1 of every 3 cycles, through Cycle 24 (1 cycle=28 days) in combination with umbralisib, 800 mg, orally, once daily, through Cycles 1-24 or until disease progression, unacceptable toxicity or withdrawal from the study for other reasons.                                                                  |                                                           |
| Reporting group title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | Arm B: Umbralisib (TGR-1202) Monotherapy                  |
| Reporting group description:<br>Subjects with FL, SLL, MZL, MCL, and DLBCL received umbralisib 800 mg orally, once daily through Cycles 1-24 (1 cycle=28 days), or until disease progression, unacceptable toxicity, or withdrawal from the study for other reasons.                                                                                                                                                                                                                                                                 |                                                           |
| Reporting group title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | Arm C: Ublituximab + Umbralisib (TGR-1202) + Bendamustine |
| Reporting group description:<br>Subjects with DLBCL received ublituximab 900 mg, IV infusion, on Days 1, 8, and 15 of Cycle 1, Day 1 of Cycles 2-6 and, thereafter on Day 1 of every 3 cycles, through Cycle 24 (1 cycle=28 days) in combination with umbralisib, 800 mg orally, once daily through Cycles 1-24 and bendamustine 90 milligrams per square meter (mg/m <sup>2</sup> ), IV infusion, on Days 1 and 2 of Cycles 1-6 or until disease progression, unacceptable toxicity or withdrawal from the study for other reasons. |                                                           |
| Reporting group title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | Arm D: Ublituximab Monotherapy                            |
| Reporting group description:<br>Subjects with FL received ublituximab 900 mg, IV infusion, on Days 1, 8, and 15 of Cycle 1, Day 1 of Cycles 2-6 and, thereafter on Day 1 of every 3 cycles, through Cycle 24 (1 cycle=28 days) or until disease progression, unacceptable toxicity, or withdrawal from the study for other reasons.                                                                                                                                                                                                  |                                                           |
| Reporting group title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | Arm E: Ublituximab to Umbralisib (TGR-1202)               |
| Reporting group description:<br>Subjects in Arm D were crossed over to umbralisib monotherapy upon confirmation of progressive disease (PD) by the independent review committee (IRC) to receive umbralisib, 800 mg orally, once daily, through Cycles 1-24 (1 cycle=28 days) or until disease progression, unacceptable toxicity, or withdrawal from the study for other reasons.                                                                                                                                                   |                                                           |

### Primary: Overall Response Rate (ORR)

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |                                            |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------|
| End point title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | Overall Response Rate (ORR) <sup>[1]</sup> |
| End point description:<br>The ORR was defined as the sum of the percentage of subjects who had complete response (CR) and partial response (PR) and was determined according to the Revised Criteria for Malignant Lymphoma (Cheson 2007). CR was defined as the disappearance of all evidence of disease, spleen &/or liver normal in size, disappearance of all nodules of disease, all lymph nodes and nodal masses in fluorodeoxyglucose (FDG) avid lymphomas regressed to normal size. PR was defined as the regression of measurable disease and no new sites of disease. Regression was $\geq 50\%$ decrease in sum of the products of diameters (SPD) of index lesions, with no unequivocal increase in size of other lymph nodes, liver, or spleen. Data for this endpoint was not collected or analysed as the study was terminated due to the sponsor's business decision. |                                            |
| End point type                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | Primary                                    |
| End point timeframe:<br>Up to approximately 6 years                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                            |
| Notes:<br>[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.<br>Justification: Data for this endpoint was not collected or analysed as the study was terminated due to the sponsor's business decision.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                            |

| End point values                 | Arm A:<br>Ublituximab +<br>Umbralisib<br>(TGR-1202) | Arm B:<br>Umbralisib<br>(TGR-1202)<br>Monotherapy | Arm C:<br>Ublituximab +<br>Umbralisib<br>(TGR-1202) +<br>Bendamustine | Arm D:<br>Ublituximab<br>Monotherapy |
|----------------------------------|-----------------------------------------------------|---------------------------------------------------|-----------------------------------------------------------------------|--------------------------------------|
| Subject group type               | Reporting group                                     | Reporting group                                   | Reporting group                                                       | Reporting group                      |
| Number of subjects analysed      | 0 <sup>[2]</sup>                                    | 0 <sup>[3]</sup>                                  | 0 <sup>[4]</sup>                                                      | 0 <sup>[5]</sup>                     |
| Units: percentage of subjects    |                                                     |                                                   |                                                                       |                                      |
| number (confidence interval 95%) | ( to )                                              | ( to )                                            | ( to )                                                                | ( to )                               |

Notes:

[2] - Data was not collected or analysed due to the termination of the study by the sponsor.

[3] - Data was not collected or analysed due to the termination of the study by the sponsor.

[4] - Data was not collected or analysed due to the termination of the study by the sponsor.

[5] - Data was not collected or analysed due to the termination of the study by the sponsor.

| End point values                 | Arm E:<br>Ublituximab to<br>Umbralisib<br>(TGR-1202) |  |  |  |
|----------------------------------|------------------------------------------------------|--|--|--|
| Subject group type               | Reporting group                                      |  |  |  |
| Number of subjects analysed      | 0 <sup>[6]</sup>                                     |  |  |  |
| Units: percentage of subjects    |                                                      |  |  |  |
| number (confidence interval 95%) | ( to )                                               |  |  |  |

Notes:

[6] - Data was not collected or analysed due to the termination of the study by the sponsor.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Progression-Free Survival (PFS)

|                 |                                 |
|-----------------|---------------------------------|
| End point title | Progression-Free Survival (PFS) |
|-----------------|---------------------------------|

End point description:

PFS was defined as the interval from randomisation to the earlier of the first documentation of definitive disease progression or death from any cause. The appearance of any new lesion more than 1.5 centimeters (cm) in any axis, even if other lesions were decreasing in size was considered relapsed or progressive disease. At least a 50% increase from nadir in one of the following: SPD of index lesions, greatest transverse diameter (GTD) of any individual previously involved node, or GTD of any previously involved node provided that the GTD of that node was  $\geq 1.5$  cm. Data for this endpoint was not collected or analysed as the study was terminated due to the sponsor's business decision.

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

End point timeframe:

From date of randomisation until the date of first documented progression or death (up to approximately 6 years)

| End point values                 | Arm A:<br>Ublituximab +<br>Umbralisib<br>(TGR-1202) | Arm B:<br>Umbralisib<br>(TGR-1202)<br>Monotherapy | Arm C:<br>Ublituximab +<br>Umbralisib<br>(TGR-1202) +<br>Bendamustine | Arm D:<br>Ublituximab<br>Monotherapy |
|----------------------------------|-----------------------------------------------------|---------------------------------------------------|-----------------------------------------------------------------------|--------------------------------------|
| Subject group type               | Reporting group                                     | Reporting group                                   | Reporting group                                                       | Reporting group                      |
| Number of subjects analysed      | 0 <sup>[7]</sup>                                    | 0 <sup>[8]</sup>                                  | 0 <sup>[9]</sup>                                                      | 0 <sup>[10]</sup>                    |
| Units: months                    |                                                     |                                                   |                                                                       |                                      |
| number (confidence interval 95%) | ( to )                                              | ( to )                                            | ( to )                                                                | ( to )                               |

Notes:

- [7] - Data was not collected or analysed due to the termination of the study by the sponsor.  
[8] - Data was not collected or analysed due to the termination of the study by the sponsor.  
[9] - Data was not collected or analysed due to the termination of the study by the sponsor.  
[10] - Data was not collected or analysed due to the termination of the study by the sponsor.

| End point values                 | Arm E:<br>Ublituximab to<br>Umbralisib<br>(TGR-1202) |  |  |  |
|----------------------------------|------------------------------------------------------|--|--|--|
| Subject group type               | Reporting group                                      |  |  |  |
| Number of subjects analysed      | 0 <sup>[11]</sup>                                    |  |  |  |
| Units: months                    |                                                      |  |  |  |
| number (confidence interval 95%) | ( to )                                               |  |  |  |

Notes:

- [11] - Data was not collected or analysed due to the termination of the study by the sponsor.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Progression-Free Survival (PFS) at Month 6

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                                            |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------|
| End point title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | Progression-Free Survival (PFS) at Month 6 |
| End point description:<br>PFS was defined as the percentage of subjects not experiencing progression i.e definitive disease progression or death from any cause by Month 6. The appearance of any new lesion more than 1.5 cm in any axis, even if other lesions were decreasing in size was considered relapsed or progressive disease. At least a 50% increase from nadir in one of the following: SPD of index lesions, GTD of any individual previously involved node, or GTD of any previously involved node provided that the GTD of that node was $\geq 1.5$ cm. Data for this endpoint was not collected or analysed as the study was terminated due to the sponsor's business decision. |                                            |
| End point type                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | Secondary                                  |
| End point timeframe:<br>At Month 6                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                            |

| End point values                 | Arm A:<br>Ublituximab +<br>Umbralisib<br>(TGR-1202) | Arm B:<br>Umbralisib<br>(TGR-1202)<br>Monotherapy | Arm C:<br>Ublituximab +<br>Umbralisib<br>(TGR-1202) +<br>Bendamustine | Arm D:<br>Ublituximab<br>Monotherapy |
|----------------------------------|-----------------------------------------------------|---------------------------------------------------|-----------------------------------------------------------------------|--------------------------------------|
| Subject group type               | Reporting group                                     | Reporting group                                   | Reporting group                                                       | Reporting group                      |
| Number of subjects analysed      | 0 <sup>[12]</sup>                                   | 0 <sup>[13]</sup>                                 | 0 <sup>[14]</sup>                                                     | 0 <sup>[15]</sup>                    |
| Units: percentage of subjects    |                                                     |                                                   |                                                                       |                                      |
| number (confidence interval 95%) | ( to )                                              | ( to )                                            | ( to )                                                                | ( to )                               |

Notes:

- [12] - Data was not collected or analysed due to the termination of the study by the sponsor.  
[13] - Data was not collected or analysed due to the termination of the study by the sponsor.  
[14] - Data was not collected or analysed due to the termination of the study by the sponsor.  
[15] - Data was not collected or analysed due to the termination of the study by the sponsor.

| End point values | Arm E:<br>Ublituximab to<br>Umbralisib |  |  |  |
|------------------|----------------------------------------|--|--|--|
|------------------|----------------------------------------|--|--|--|

|                                  |                   |  |  |  |
|----------------------------------|-------------------|--|--|--|
|                                  | (TGR-1202)        |  |  |  |
| Subject group type               | Reporting group   |  |  |  |
| Number of subjects analysed      | 0 <sup>[16]</sup> |  |  |  |
| Units: percentage of subjects    |                   |  |  |  |
| number (confidence interval 95%) | ( to )            |  |  |  |

Notes:

[16] - Data was not collected or analysed due to the termination of the study by the sponsor.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Complete Response (CR) Rate

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                             |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------|
| End point title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | Complete Response (CR) Rate |
| End point description:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |                             |
| CR rate is defined as the percentage of subjects who achieve a CR as determined according to the Revised Criteria for Malignant Lymphoma (Cheson 2007). CR was defined as the disappearance of all evidence of disease, spleen &/or liver normal in size, disappearance of all nodules of disease, all lymph nodes and nodal masses in FDG-avid lymphomas regressed to normal size. Data for this endpoint was not collected or analysed as the study was terminated due to the sponsor's business decision. |                             |
| End point type                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | Secondary                   |
| End point timeframe:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                             |
| Up to approximately 6 years                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                             |

| End point values                 | Arm A:<br>Ublituximab +<br>Umbralisib<br>(TGR-1202) | Arm B:<br>Umbralisib<br>(TGR-1202)<br>Monotherapy | Arm C:<br>Ublituximab +<br>Umbralisib<br>(TGR-1202) +<br>Bendamustine | Arm D:<br>Ublituximab<br>Monotherapy |
|----------------------------------|-----------------------------------------------------|---------------------------------------------------|-----------------------------------------------------------------------|--------------------------------------|
| Subject group type               | Reporting group                                     | Reporting group                                   | Reporting group                                                       | Reporting group                      |
| Number of subjects analysed      | 0 <sup>[17]</sup>                                   | 0 <sup>[18]</sup>                                 | 0 <sup>[19]</sup>                                                     | 0 <sup>[20]</sup>                    |
| Units: percentage of subjects    |                                                     |                                                   |                                                                       |                                      |
| number (confidence interval 95%) | ( to )                                              | ( to )                                            | ( to )                                                                | ( to )                               |

Notes:

[17] - Data was not collected or analysed due to the termination of the study by the sponsor.

[18] - Data was not collected or analysed due to the termination of the study by the sponsor.

[19] - Data was not collected or analysed due to the termination of the study by the sponsor.

[20] - Data was not collected or analysed due to the termination of the study by the sponsor.

| End point values                 | Arm E:<br>Ublituximab to<br>Umbralisib<br>(TGR-1202) |  |  |  |
|----------------------------------|------------------------------------------------------|--|--|--|
| Subject group type               | Reporting group                                      |  |  |  |
| Number of subjects analysed      | 0 <sup>[21]</sup>                                    |  |  |  |
| Units: percentage of subjects    |                                                      |  |  |  |
| number (confidence interval 95%) | ( to )                                               |  |  |  |

Notes:

[21] - Data was not collected or analysed due to the termination of the study by the sponsor.

## Statistical analyses

No statistical analyses for this end point

### Secondary: Overall Survival (OS)

|                 |                       |
|-----------------|-----------------------|
| End point title | Overall Survival (OS) |
|-----------------|-----------------------|

End point description:

OS is defined as the interval from randomisation to death from any cause. Data for this endpoint was not collected or analysed as the study was terminated due to the sponsor's business decision.

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

End point timeframe:

Up to approximately 6 years

| End point values                 | Arm A:<br>Ublituximab +<br>Umbralisib<br>(TGR-1202) | Arm B:<br>Umbralisib<br>(TGR-1202)<br>Monotherapy | Arm C:<br>Ublituximab +<br>Umbralisib<br>(TGR-1202) +<br>Bendamustine | Arm D:<br>Ublituximab<br>Monotherapy |
|----------------------------------|-----------------------------------------------------|---------------------------------------------------|-----------------------------------------------------------------------|--------------------------------------|
| Subject group type               | Reporting group                                     | Reporting group                                   | Reporting group                                                       | Reporting group                      |
| Number of subjects analysed      | 0 <sup>[22]</sup>                                   | 0 <sup>[23]</sup>                                 | 0 <sup>[24]</sup>                                                     | 0 <sup>[25]</sup>                    |
| Units: months                    |                                                     |                                                   |                                                                       |                                      |
| number (confidence interval 95%) | ( to )                                              | ( to )                                            | ( to )                                                                | ( to )                               |

Notes:

[22] - Data was not collected or analysed due to the termination of the study by the sponsor.

[23] - Data was not collected or analysed due to the termination of the study by the sponsor.

[24] - Data was not collected or analysed due to the termination of the study by the sponsor.

[25] - Data was not collected or analysed due to the termination of the study by the sponsor.

| End point values                 | Arm E:<br>Ublituximab to<br>Umbralisib<br>(TGR-1202) |  |  |  |
|----------------------------------|------------------------------------------------------|--|--|--|
| Subject group type               | Reporting group                                      |  |  |  |
| Number of subjects analysed      | 0 <sup>[26]</sup>                                    |  |  |  |
| Units: months                    |                                                      |  |  |  |
| number (confidence interval 95%) | ( to )                                               |  |  |  |

Notes:

[26] - Data was not collected or analysed due to the termination of the study by the sponsor.

## Statistical analyses

No statistical analyses for this end point

### Secondary: Duration of Response (DOR)

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

End point description:

DOR is defined as the interval from the first documentation of CR or PR to the earlier of the first documentation of definitive disease progression or death from any cause. CR=disappearance of all evidence of disease, spleen &/or liver normal in size, disappearance of all nodules of disease, all lymph nodes and nodal masses in FDG-avid lymphomas regressed to normal size. PR=regression of measurable disease and no new sites of disease. Regression= $\geq 50\%$  decrease in SPD of index lesions, with no unequivocal increase in size of other lymph nodes, liver, or spleen. PD=appearance of any new lesion

more than 1.5 cm in any axis, even if other lesions were decreasing in size. At least a 50% increase from nadir in one of the following: SPD of index lesions, GTD of any individual previously involved node, or GTD of any previously involved node provided that the GTD of that node was  $\geq 1.5$  cm. Data for this endpoint was not collected/analysed as the study was terminated due to the sponsor's decision.

|                             |           |
|-----------------------------|-----------|
| End point type              | Secondary |
| End point timeframe:        |           |
| Up to approximately 6 years |           |

| End point values              | Arm A:<br>Ublituximab +<br>Umbralisib<br>(TGR-1202) | Arm B:<br>Umbralisib<br>(TGR-1202)<br>Monotherapy | Arm C:<br>Ublituximab +<br>Umbralisib<br>(TGR-1202) +<br>Bendamustine | Arm D:<br>Ublituximab<br>Monotherapy |
|-------------------------------|-----------------------------------------------------|---------------------------------------------------|-----------------------------------------------------------------------|--------------------------------------|
| Subject group type            | Reporting group                                     | Reporting group                                   | Reporting group                                                       | Reporting group                      |
| Number of subjects analysed   | 0 <sup>[27]</sup>                                   | 0 <sup>[28]</sup>                                 | 0 <sup>[29]</sup>                                                     | 0 <sup>[30]</sup>                    |
| Units: months                 |                                                     |                                                   |                                                                       |                                      |
| median (full range (min-max)) | ( to )                                              | ( to )                                            | ( to )                                                                | ( to )                               |

Notes:

[27] - Data was not collected or analysed due to the termination of the study by the sponsor.

[28] - Data was not collected or analysed due to the termination of the study by the sponsor.

[29] - Data was not collected or analysed due to the termination of the study by the sponsor.

[30] - Data was not collected or analysed due to the termination of the study by the sponsor.

| End point values              | Arm E:<br>Ublituximab to<br>Umbralisib<br>(TGR-1202) |  |  |  |
|-------------------------------|------------------------------------------------------|--|--|--|
| Subject group type            | Reporting group                                      |  |  |  |
| Number of subjects analysed   | 0 <sup>[31]</sup>                                    |  |  |  |
| Units: months                 |                                                      |  |  |  |
| median (full range (min-max)) | ( to )                                               |  |  |  |

Notes:

[31] - Data was not collected or analysed due to the termination of the study by the sponsor.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Subjects With Treatment Emergent Adverse Events (TEAEs)

|                 |                                                                   |
|-----------------|-------------------------------------------------------------------|
| End point title | Number of Subjects With Treatment Emergent Adverse Events (TEAEs) |
|-----------------|-------------------------------------------------------------------|

End point description:

An adverse event (AE) is any untoward medical occurrence in a subject or clinical investigation subject administered a pharmaceutical product. An AE does not necessarily have a causal relationship with this treatment. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding, for example), symptom, or disease temporarily associated with the use of a medicinal product, whether or not considered related to the medicinal product. TEAE is any AE that occur after first dosing of study medication and through the end of the study or through 30 days after the last dose of study treatment, or is considered treatment-related regardless of the start date of the event, or is present before first dosing of study medication but worsens in intensity or the investigator subsequently considers treatment-related. Safety Population included all subjects who were enrolled and received at least one dose of the study drug.

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

---

End point timeframe:

Up to approximately 6 years

---

| <b>End point values</b>     | Arm A:<br>Ublituximab +<br>Umbralisib<br>(TGR-1202) | Arm B:<br>Umbralisib<br>(TGR-1202)<br>Monotherapy | Arm C:<br>Ublituximab +<br>Umbralisib<br>(TGR-1202) +<br>Bendamustine | Arm D:<br>Ublituximab<br>Monotherapy |
|-----------------------------|-----------------------------------------------------|---------------------------------------------------|-----------------------------------------------------------------------|--------------------------------------|
| Subject group type          | Reporting group                                     | Reporting group                                   | Reporting group                                                       | Reporting group                      |
| Number of subjects analysed | 262                                                 | 307                                               | 130                                                                   | 24                                   |
| Units: Subjects             | 255                                                 | 303                                               | 127                                                                   | 21                                   |

| <b>End point values</b>     | Arm E:<br>Ublituximab to<br>Umbralisib<br>(TGR-1202) |  |  |  |
|-----------------------------|------------------------------------------------------|--|--|--|
| Subject group type          | Reporting group                                      |  |  |  |
| Number of subjects analysed | 12                                                   |  |  |  |
| Units: Subjects             | 12                                                   |  |  |  |

### Statistical analyses

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No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

From signing of informed consent until 30 days after last dose of study drug (up to approximately 6 years)

Adverse event reporting additional description:

Safety Population included all subjects who were enrolled and received at least one dose of the study drug.

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

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 23.0 |
|--------------------|------|

### Reporting groups

|                       |                                            |
|-----------------------|--------------------------------------------|
| Reporting group title | Arm A: Ublituximab + Umbralisib (TGR-1202) |
|-----------------------|--------------------------------------------|

Reporting group description:

Subjects with FL, MZL, MCL, and DLBCL received ublituximab, 900 mg, IV, infusion on Days 1, 8, and 15 of Cycle 1, Day 1 of Cycles 2-6, and thereafter on Day 1 of every 3 cycles, through Cycle 24 (1 cycle=28 days) in combination with umbralisib, 800 mg, orally, once daily, through Cycles 1-24 or until disease progression, unacceptable toxicity or withdrawal from the study for other reasons.

|                       |                                          |
|-----------------------|------------------------------------------|
| Reporting group title | Arm B: Umbralisib (TGR-1202) Monotherapy |
|-----------------------|------------------------------------------|

Reporting group description:

Subjects with FL, SLL, MZL, MCL, and DLBCL received umbralisib 800 mg orally, once daily through Cycles 1-24 (1 cycle=28 days), or until disease progression, unacceptable toxicity, or withdrawal from the study for other reasons.

|                       |                                                           |
|-----------------------|-----------------------------------------------------------|
| Reporting group title | Arm C: Ublituximab + Umbralisib (TGR-1202) + Bendamustine |
|-----------------------|-----------------------------------------------------------|

Reporting group description:

Subjects with DLBCL received ublituximab 900 mg, IV infusion, on Days 1, 8, and 15 of Cycle 1, Day 1 of Cycles 2-6 and, thereafter on Day 1 of every 3 cycles, through Cycle 24 (1 cycle=28 days) in combination with umbralisib, 800 mg orally, once daily through Cycles 1-24 and bendamustine 90 mg/m<sup>2</sup>, IV infusion, on Days 1 and 2 of Cycles 1-6 or until disease progression, unacceptable toxicity or withdrawal from the study for other reasons.

|                       |                                |
|-----------------------|--------------------------------|
| Reporting group title | Arm D: Ublituximab Monotherapy |
|-----------------------|--------------------------------|

Reporting group description:

Subjects with FL received ublituximab 900 mg, IV infusion, on Days 1, 8, and 15 of Cycle 1, Day 1 of Cycles 2-6 and, thereafter on Day 1 of every 3 cycles, through Cycle 24 (1 cycle=28 days) or until disease progression, unacceptable toxicity, or withdrawal from the study for other reasons.

|                       |                                             |
|-----------------------|---------------------------------------------|
| Reporting group title | Arm E: Ublituximab to Umbralisib (TGR-1202) |
|-----------------------|---------------------------------------------|

Reporting group description:

Subjects in Arm D were crossed over to umbralisib monotherapy upon confirmation of PD by the IRC to receive umbralisib, 800 mg orally, once daily, through Cycles 1-24 (1 cycle=28 days) or until disease progression, unacceptable toxicity, or withdrawal from the study for other reasons.

| Serious adverse events                            | Arm A: Ublituximab + Umbralisib (TGR-1202) | Arm B: Umbralisib (TGR-1202) Monotherapy | Arm C: Ublituximab + Umbralisib (TGR-1202) + Bendamustine |
|---------------------------------------------------|--------------------------------------------|------------------------------------------|-----------------------------------------------------------|
| Total subjects affected by serious adverse events |                                            |                                          |                                                           |
| subjects affected / exposed                       | 108 / 262 (41.22%)                         | 106 / 307 (34.53%)                       | 63 / 130 (48.46%)                                         |
| number of deaths (all causes)                     | 73                                         | 54                                       | 88                                                        |
| number of deaths resulting from adverse events    | 3                                          | 2                                        | 2                                                         |

|                                                                     |                 |                 |                 |
|---------------------------------------------------------------------|-----------------|-----------------|-----------------|
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                 |                 |                 |
| Adenocarcinoma pancreas                                             |                 |                 |                 |
| subjects affected / exposed                                         | 1 / 262 (0.38%) | 1 / 307 (0.33%) | 0 / 130 (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           |
| Breast cancer recurrent                                             |                 |                 |                 |
| subjects affected / exposed                                         | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (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 adenocarcinoma                                     |                 |                 |                 |
| subjects affected / exposed                                         | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (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           |
| Infected neoplasm                                                   |                 |                 |                 |
| subjects affected / exposed                                         | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (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           |
| Intraductal proliferative breast lesion                             |                 |                 |                 |
| subjects affected / exposed                                         | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (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           |
| Invasive ductal breast carcinoma                                    |                 |                 |                 |
| subjects affected / exposed                                         | 1 / 262 (0.38%) | 1 / 307 (0.33%) | 0 / 130 (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           |
| Neuroendocrine carcinoma of the skin                                |                 |                 |                 |
| subjects affected / exposed                                         | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences causally related to treatment / all                     | 0 / 1           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all                          | 0 / 0           | 0 / 0           | 0 / 0           |
| Anal cancer                                                         |                 |                 |                 |
| subjects affected / exposed                                         | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (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           |

|                                                      |                 |                 |                 |
|------------------------------------------------------|-----------------|-----------------|-----------------|
| Extranodal marginal zone B-cell lymphoma (MALT type) |                 |                 |                 |
| subjects affected / exposed                          | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (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           |
| Gastrointestinal neoplasm                            |                 |                 |                 |
| subjects affected / exposed                          | 0 / 262 (0.00%) | 0 / 307 (0.00%) | 1 / 130 (0.77%) |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           | 0 / 0           |
| Glioma                                               |                 |                 |                 |
| subjects affected / exposed                          | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (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           |
| Lymphoma                                             |                 |                 |                 |
| subjects affected / exposed                          | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 2           | 0 / 0           |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           | 0 / 0           |
| Malignant melanoma in situ                           |                 |                 |                 |
| subjects affected / exposed                          | 0 / 262 (0.00%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           | 0 / 0           |
| Myelodysplastic syndrome                             |                 |                 |                 |
| subjects affected / exposed                          | 0 / 262 (0.00%) | 0 / 307 (0.00%) | 2 / 130 (1.54%) |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 0           | 2 / 2           |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           | 0 / 0           |
| Squamous cell carcinoma                              |                 |                 |                 |
| subjects affected / exposed                          | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 2           | 0 / 0           |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           | 0 / 0           |
| Squamous cell carcinoma of lung                      |                 |                 |                 |
| subjects affected / exposed                          | 0 / 262 (0.00%) | 0 / 307 (0.00%) | 1 / 130 (0.77%) |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           | 0 / 0           |
| Squamous cell carcinoma of skin                      |                 |                 |                 |

|                                                  |                 |                 |                 |
|--------------------------------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed                      | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (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           |
| Superficial spreading melanoma stage unspecified |                 |                 |                 |
| subjects affected / exposed                      | 0 / 262 (0.00%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| 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                      | 3 / 262 (1.15%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences causally related to treatment / all  | 0 / 3           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all       | 0 / 0           | 0 / 0           | 0 / 0           |
| Deep vein thrombosis                             |                 |                 |                 |
| subjects affected / exposed                      | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (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           |
| Embolism                                         |                 |                 |                 |
| subjects affected / exposed                      | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (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           |
| Circulatory collapse                             |                 |                 |                 |
| subjects affected / exposed                      | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (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           |
| Orthostatic hypotension                          |                 |                 |                 |
| subjects affected / exposed                      | 0 / 262 (0.00%) | 0 / 307 (0.00%) | 2 / 130 (1.54%) |
| occurrences causally related to treatment / all  | 0 / 0           | 0 / 0           | 0 / 2           |
| deaths causally related to treatment / all       | 0 / 0           | 0 / 0           | 0 / 0           |
| Peripheral ischaemia                             |                 |                 |                 |
| subjects affected / exposed                      | 0 / 262 (0.00%) | 0 / 307 (0.00%) | 1 / 130 (0.77%) |
| occurrences causally related to treatment / all  | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all       | 0 / 0           | 0 / 0           | 0 / 0           |
| Surgical and medical procedures                  |                 |                 |                 |

|                                                      |                 |                 |                 |
|------------------------------------------------------|-----------------|-----------------|-----------------|
| Alcohol detoxification                               |                 |                 |                 |
| subjects affected / exposed                          | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 1           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           | 0 / 0           |
| Catheter placement                                   |                 |                 |                 |
| subjects affected / exposed                          | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (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           |
| Fluid replacement                                    |                 |                 |                 |
| subjects affected / exposed                          | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (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           |
| Hip arthroplasty                                     |                 |                 |                 |
| subjects affected / exposed                          | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (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 |                 |                 |                 |
| Chest pain                                           |                 |                 |                 |
| subjects affected / exposed                          | 1 / 262 (0.38%) | 1 / 307 (0.33%) | 0 / 130 (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           |
| Death                                                |                 |                 |                 |
| subjects affected / exposed                          | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (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           |
| Fatigue                                              |                 |                 |                 |
| subjects affected / exposed                          | 1 / 262 (0.38%) | 1 / 307 (0.33%) | 1 / 130 (0.77%) |
| occurrences causally related to treatment / all      | 1 / 1           | 0 / 1           | 1 / 1           |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           | 0 / 0           |
| Incarcerated hernia                                  |                 |                 |                 |
| subjects affected / exposed                          | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 1           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           | 0 / 0           |

|                                                 |                 |                 |                 |
|-------------------------------------------------|-----------------|-----------------|-----------------|
| Multiple organ dysfunction syndrome             |                 |                 |                 |
| subjects affected / exposed                     | 1 / 262 (0.38%) | 1 / 307 (0.33%) | 0 / 130 (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           |
| Pain                                            |                 |                 |                 |
| subjects affected / exposed                     | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (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 / 262 (0.38%) | 3 / 307 (0.98%) | 5 / 130 (3.85%) |
| occurrences causally related to treatment / all | 1 / 1           | 1 / 4           | 4 / 8           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Asthenia                                        |                 |                 |                 |
| subjects affected / exposed                     | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 1 / 130 (0.77%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Hypothermia                                     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (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           |
| Non-cardiac chest pain                          |                 |                 |                 |
| subjects affected / exposed                     | 0 / 262 (0.00%) | 0 / 307 (0.00%) | 1 / 130 (0.77%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 1 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Reproductive system and breast disorders        |                 |                 |                 |
| Vaginal fistula                                 |                 |                 |                 |
| subjects affected / exposed <sup>[1]</sup>      | 1 / 105 (0.95%) | 0 / 139 (0.00%) | 0 / 52 (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           |
| Penile pain                                     |                 |                 |                 |
| subjects affected / exposed <sup>[2]</sup>      | 0 / 157 (0.00%) | 1 / 168 (0.60%) | 0 / 78 (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           |

|                                                 |                 |                 |                 |
|-------------------------------------------------|-----------------|-----------------|-----------------|
| Respiratory, thoracic and mediastinal disorders |                 |                 |                 |
| Dyspnoea                                        |                 |                 |                 |
| subjects affected / exposed                     | 4 / 262 (1.53%) | 3 / 307 (0.98%) | 1 / 130 (0.77%) |
| occurrences causally related to treatment / all | 0 / 4           | 0 / 4           | 1 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Respiratory failure                             |                 |                 |                 |
| subjects affected / exposed                     | 3 / 262 (1.15%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences causally related to treatment / all | 0 / 3           | 0 / 1           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Chronic obstructive pulmonary disease           |                 |                 |                 |
| subjects affected / exposed                     | 2 / 262 (0.76%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 1           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Hypoxia                                         |                 |                 |                 |
| subjects affected / exposed                     | 2 / 262 (0.76%) | 0 / 307 (0.00%) | 1 / 130 (0.77%) |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 0           | 1 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Pleural effusion                                |                 |                 |                 |
| subjects affected / exposed                     | 1 / 262 (0.38%) | 4 / 307 (1.30%) | 1 / 130 (0.77%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 4           | 1 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Pneumonia aspiration                            |                 |                 |                 |
| subjects affected / exposed                     | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (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           |
| Pneumonitis                                     |                 |                 |                 |
| subjects affected / exposed                     | 1 / 262 (0.38%) | 4 / 307 (1.30%) | 1 / 130 (0.77%) |
| occurrences causally related to treatment / all | 1 / 1           | 2 / 4           | 1 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Pulmonary congestion                            |                 |                 |                 |
| subjects affected / exposed                     | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (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           |

|                                                 |                 |                 |                 |
|-------------------------------------------------|-----------------|-----------------|-----------------|
| Pulmonary oedema                                |                 |                 |                 |
| subjects affected / exposed                     | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (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           |
| Acute respiratory distress syndrome             |                 |                 |                 |
| subjects affected / exposed                     | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (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           |
| Acute respiratory failure                       |                 |                 |                 |
| subjects affected / exposed                     | 0 / 262 (0.00%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Cough                                           |                 |                 |                 |
| subjects affected / exposed                     | 0 / 262 (0.00%) | 0 / 307 (0.00%) | 1 / 130 (0.77%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Epistaxis                                       |                 |                 |                 |
| subjects affected / exposed                     | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (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           |
| Interstitial lung disease                       |                 |                 |                 |
| subjects affected / exposed                     | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (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           |
| Pulmonary embolism                              |                 |                 |                 |
| subjects affected / exposed                     | 0 / 262 (0.00%) | 2 / 307 (0.65%) | 0 / 130 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 2           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Psychiatric disorders                           |                 |                 |                 |
| Confusional state                               |                 |                 |                 |
| subjects affected / exposed                     | 2 / 262 (0.76%) | 0 / 307 (0.00%) | 0 / 130 (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           |
| Bipolar disorder                                |                 |                 |                 |

|                                                 |                 |                 |                 |
|-------------------------------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed                     | 0 / 262 (0.00%) | 0 / 307 (0.00%) | 1 / 130 (0.77%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Mental status changes                           |                 |                 |                 |
| subjects affected / exposed                     | 0 / 262 (0.00%) | 2 / 307 (0.65%) | 1 / 130 (0.77%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 2           | 1 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Investigations                                  |                 |                 |                 |
| Alanine aminotransferase increased              |                 |                 |                 |
| subjects affected / exposed                     | 2 / 262 (0.76%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences causally related to treatment / all | 2 / 2           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Aspartate aminotransferase increased            |                 |                 |                 |
| subjects affected / exposed                     | 2 / 262 (0.76%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences causally related to treatment / all | 2 / 2           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Blood bilirubin increased                       |                 |                 |                 |
| subjects affected / exposed                     | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 1 / 130 (0.77%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Hepatic enzyme increased                        |                 |                 |                 |
| subjects affected / exposed                     | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (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           |
| Transaminases increased                         |                 |                 |                 |
| subjects affected / exposed                     | 1 / 262 (0.38%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1           | 1 / 1           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Blood creatinine increased                      |                 |                 |                 |
| subjects affected / exposed                     | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (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           |
| Neutrophil count decreased                      |                 |                 |                 |

|                                                 |                 |                 |                 |
|-------------------------------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed                     | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 1 / 130 (0.77%) |
| occurrences causally related to treatment / all | 0 / 0           | 1 / 1           | 1 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Injury, poisoning and procedural complications  |                 |                 |                 |
| Infusion related reaction                       |                 |                 |                 |
| subjects affected / exposed                     | 4 / 262 (1.53%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences causally related to treatment / all | 4 / 4           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Fall                                            |                 |                 |                 |
| subjects affected / exposed                     | 2 / 262 (0.76%) | 0 / 307 (0.00%) | 1 / 130 (0.77%) |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Arterial injury                                 |                 |                 |                 |
| subjects affected / exposed                     | 1 / 262 (0.38%) | 1 / 307 (0.33%) | 0 / 130 (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           |
| Hip fracture                                    |                 |                 |                 |
| subjects affected / exposed                     | 1 / 262 (0.38%) | 2 / 307 (0.65%) | 3 / 130 (2.31%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 2           | 0 / 3           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Alcohol poisoning                               |                 |                 |                 |
| subjects affected / exposed                     | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (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           |
| Arthropod bite                                  |                 |                 |                 |
| subjects affected / exposed                     | 0 / 262 (0.00%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Brain contusion                                 |                 |                 |                 |
| subjects affected / exposed                     | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (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           |
| Contusion                                       |                 |                 |                 |

|                                                 |                 |                 |                 |
|-------------------------------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed                     | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (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           |
| Femur fracture                                  |                 |                 |                 |
| subjects affected / exposed                     | 0 / 262 (0.00%) | 2 / 307 (0.65%) | 0 / 130 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 2           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Lower limb fracture                             |                 |                 |                 |
| subjects affected / exposed                     | 0 / 262 (0.00%) | 0 / 307 (0.00%) | 1 / 130 (0.77%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Overdose                                        |                 |                 |                 |
| subjects affected / exposed                     | 0 / 262 (0.00%) | 0 / 307 (0.00%) | 1 / 130 (0.77%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Pelvic fracture                                 |                 |                 |                 |
| subjects affected / exposed                     | 0 / 262 (0.00%) | 0 / 307 (0.00%) | 1 / 130 (0.77%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Spinal compression fracture                     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Spinal fracture                                 |                 |                 |                 |
| subjects affected / exposed                     | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (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           |
| Splenic rupture                                 |                 |                 |                 |
| subjects affected / exposed                     | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Cardiac disorders                               |                 |                 |                 |
| Cardiac failure                                 |                 |                 |                 |

|                                                 |                 |                 |                 |
|-------------------------------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed                     | 4 / 262 (1.53%) | 2 / 307 (0.65%) | 0 / 130 (0.00%) |
| occurrences causally related to treatment / all | 2 / 5           | 0 / 2           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Cardiac arrest                                  |                 |                 |                 |
| subjects affected / exposed                     | 2 / 262 (0.76%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Cardiac failure congestive                      |                 |                 |                 |
| subjects affected / exposed                     | 2 / 262 (0.76%) | 1 / 307 (0.33%) | 1 / 130 (0.77%) |
| occurrences causally related to treatment / all | 1 / 2           | 0 / 1           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Cardio-respiratory arrest                       |                 |                 |                 |
| subjects affected / exposed                     | 2 / 262 (0.76%) | 0 / 307 (0.00%) | 0 / 130 (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           |
| Acute left ventricular failure                  |                 |                 |                 |
| subjects affected / exposed                     | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Acute myocardial infarction                     |                 |                 |                 |
| subjects affected / exposed                     | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (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           |
| Aortic valve disease                            |                 |                 |                 |
| subjects affected / exposed                     | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (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           |
| Atrial fibrillation                             |                 |                 |                 |
| subjects affected / exposed                     | 1 / 262 (0.38%) | 2 / 307 (0.65%) | 2 / 130 (1.54%) |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 2           | 1 / 2           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Cardiopulmonary failure                         |                 |                 |                 |

|                                                 |                 |                 |                 |
|-------------------------------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed                     | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (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           |
| Tachycardia                                     |                 |                 |                 |
| subjects affected / exposed                     | 1 / 262 (0.38%) | 2 / 307 (0.65%) | 0 / 130 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 2           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Ventricular failure                             |                 |                 |                 |
| subjects affected / exposed                     | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Acute coronary syndrome                         |                 |                 |                 |
| subjects affected / exposed                     | 0 / 262 (0.00%) | 0 / 307 (0.00%) | 1 / 130 (0.77%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Atrial flutter                                  |                 |                 |                 |
| subjects affected / exposed                     | 0 / 262 (0.00%) | 2 / 307 (0.65%) | 0 / 130 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 1 / 2           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Cardiac tamponade                               |                 |                 |                 |
| subjects affected / exposed                     | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (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           |
| Coronary artery disease                         |                 |                 |                 |
| subjects affected / exposed                     | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (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 / 262 (0.00%) | 3 / 307 (0.98%) | 0 / 130 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 3           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Pericardial effusion                            |                 |                 |                 |

|                                                 |                 |                 |                 |
|-------------------------------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed                     | 0 / 262 (0.00%) | 0 / 307 (0.00%) | 1 / 130 (0.77%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Stress cardiomyopathy                           |                 |                 |                 |
| subjects affected / exposed                     | 0 / 262 (0.00%) | 0 / 307 (0.00%) | 1 / 130 (0.77%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Supraventricular tachycardia                    |                 |                 |                 |
| subjects affected / exposed                     | 0 / 262 (0.00%) | 0 / 307 (0.00%) | 1 / 130 (0.77%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Nervous system disorders                        |                 |                 |                 |
| Seizure                                         |                 |                 |                 |
| subjects affected / exposed                     | 3 / 262 (1.15%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences causally related to treatment / all | 2 / 4           | 0 / 1           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Cerebrovascular accident                        |                 |                 |                 |
| subjects affected / exposed                     | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (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           |
| Headache                                        |                 |                 |                 |
| subjects affected / exposed                     | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (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           |
| Hyporeflexia                                    |                 |                 |                 |
| subjects affected / exposed                     | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (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           |
| Lethargy                                        |                 |                 |                 |
| subjects affected / exposed                     | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (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           |
| Dementia                                        |                 |                 |                 |

|                                                 |                 |                 |                 |
|-------------------------------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed                     | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (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           |
| Encephalopathy                                  |                 |                 |                 |
| subjects affected / exposed                     | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 1 / 1           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 1 / 1           | 0 / 0           |
| Presyncope                                      |                 |                 |                 |
| subjects affected / exposed                     | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (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           |
| Syncope                                         |                 |                 |                 |
| subjects affected / exposed                     | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 2 / 130 (1.54%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           | 0 / 3           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Transient ischaemic attack                      |                 |                 |                 |
| subjects affected / exposed                     | 0 / 262 (0.00%) | 0 / 307 (0.00%) | 1 / 130 (0.77%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Blood and lymphatic system disorders            |                 |                 |                 |
| Febrile neutropenia                             |                 |                 |                 |
| subjects affected / exposed                     | 5 / 262 (1.91%) | 3 / 307 (0.98%) | 3 / 130 (2.31%) |
| occurrences causally related to treatment / all | 4 / 5           | 3 / 3           | 3 / 4           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Thrombocytopenia                                |                 |                 |                 |
| subjects affected / exposed                     | 2 / 262 (0.76%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences causally related to treatment / all | 2 / 2           | 3 / 3           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Anaemia                                         |                 |                 |                 |
| subjects affected / exposed                     | 1 / 262 (0.38%) | 4 / 307 (1.30%) | 5 / 130 (3.85%) |
| occurrences causally related to treatment / all | 0 / 1           | 2 / 4           | 3 / 7           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Lymphadenopathy                                 |                 |                 |                 |

|                                                 |                 |                 |                 |
|-------------------------------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed                     | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (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           |
| Neutropenia                                     |                 |                 |                 |
| subjects affected / exposed                     | 1 / 262 (0.38%) | 1 / 307 (0.33%) | 1 / 130 (0.77%) |
| occurrences causally related to treatment / all | 1 / 1           | 1 / 1           | 1 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Pancytopenia                                    |                 |                 |                 |
| subjects affected / exposed                     | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 1 / 130 (0.77%) |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Agranulocytosis                                 |                 |                 |                 |
| subjects affected / exposed                     | 0 / 262 (0.00%) | 0 / 307 (0.00%) | 1 / 130 (0.77%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Autoimmune haemolytic anaemia                   |                 |                 |                 |
| subjects affected / exposed                     | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (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           |
| Haemolytic anaemia                              |                 |                 |                 |
| subjects affected / exposed                     | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (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           |
| Eye disorders                                   |                 |                 |                 |
| Diplopia                                        |                 |                 |                 |
| subjects affected / exposed                     | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (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           |
| Optic ischaemic neuropathy                      |                 |                 |                 |
| subjects affected / exposed                     | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (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           |
| Visual impairment                               |                 |                 |                 |

|                                                 |                 |                  |                 |
|-------------------------------------------------|-----------------|------------------|-----------------|
| subjects affected / exposed                     | 0 / 262 (0.00%) | 1 / 307 (0.33%)  | 0 / 130 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 1 / 1            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| <b>Gastrointestinal disorders</b>               |                 |                  |                 |
| <b>Colitis</b>                                  |                 |                  |                 |
| subjects affected / exposed                     | 4 / 262 (1.53%) | 2 / 307 (0.65%)  | 1 / 130 (0.77%) |
| occurrences causally related to treatment / all | 4 / 4           | 1 / 2            | 1 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| <b>Diarrhoea</b>                                |                 |                  |                 |
| subjects affected / exposed                     | 4 / 262 (1.53%) | 10 / 307 (3.26%) | 2 / 130 (1.54%) |
| occurrences causally related to treatment / all | 2 / 4           | 10 / 12          | 2 / 2           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| <b>Gastrointestinal haemorrhage</b>             |                 |                  |                 |
| subjects affected / exposed                     | 2 / 262 (0.76%) | 1 / 307 (0.33%)  | 1 / 130 (0.77%) |
| occurrences causally related to treatment / all | 1 / 2           | 0 / 1            | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| <b>Abdominal pain</b>                           |                 |                  |                 |
| subjects affected / exposed                     | 1 / 262 (0.38%) | 1 / 307 (0.33%)  | 1 / 130 (0.77%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1            | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| <b>Autoimmune colitis</b>                       |                 |                  |                 |
| subjects affected / exposed                     | 1 / 262 (0.38%) | 0 / 307 (0.00%)  | 0 / 130 (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           |
| <b>Bezoar</b>                                   |                 |                  |                 |
| subjects affected / exposed                     | 1 / 262 (0.38%) | 0 / 307 (0.00%)  | 0 / 130 (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>Dysphagia</b>                                |                 |                  |                 |
| subjects affected / exposed                     | 1 / 262 (0.38%) | 0 / 307 (0.00%)  | 0 / 130 (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>Gastric haemorrhage</b>                      |                 |                  |                 |

|                                                 |                 |                 |                 |
|-------------------------------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed                     | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (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           |
| Gastric perforation                             |                 |                 |                 |
| subjects affected / exposed                     | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (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           |
| Gastrointestinal obstruction                    |                 |                 |                 |
| subjects affected / exposed                     | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (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           |
| Pancreatitis                                    |                 |                 |                 |
| subjects affected / exposed                     | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (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           |
| Pancreatitis acute                              |                 |                 |                 |
| subjects affected / exposed                     | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (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           |
| Small intestinal obstruction                    |                 |                 |                 |
| subjects affected / exposed                     | 1 / 262 (0.38%) | 1 / 307 (0.33%) | 0 / 130 (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           |
| Vomiting                                        |                 |                 |                 |
| subjects affected / exposed                     | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 3 / 130 (2.31%) |
| occurrences causally related to treatment / all | 1 / 1           | 0 / 0           | 0 / 3           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Constipation                                    |                 |                 |                 |
| subjects affected / exposed                     | 0 / 262 (0.00%) | 0 / 307 (0.00%) | 1 / 130 (0.77%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Gastric ulcer                                   |                 |                 |                 |

|                                                 |                 |                 |                 |
|-------------------------------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed                     | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (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           |
| Ileus                                           |                 |                 |                 |
| subjects affected / exposed                     | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (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           |
| Large intestinal haemorrhage                    |                 |                 |                 |
| subjects affected / exposed                     | 0 / 262 (0.00%) | 0 / 307 (0.00%) | 1 / 130 (0.77%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Nausea                                          |                 |                 |                 |
| subjects affected / exposed                     | 0 / 262 (0.00%) | 0 / 307 (0.00%) | 6 / 130 (4.62%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 4 / 6           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Oesophageal stenosis                            |                 |                 |                 |
| subjects affected / exposed                     | 0 / 262 (0.00%) | 0 / 307 (0.00%) | 1 / 130 (0.77%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Oesophagitis                                    |                 |                 |                 |
| subjects affected / exposed                     | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (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           |
| Rectal haemorrhage                              |                 |                 |                 |
| subjects affected / exposed                     | 0 / 262 (0.00%) | 0 / 307 (0.00%) | 1 / 130 (0.77%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Hepatobiliary disorders                         |                 |                 |                 |
| Autoimmune hepatitis                            |                 |                 |                 |
| subjects affected / exposed                     | 0 / 262 (0.00%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Cholangitis                                     |                 |                 |                 |

|                                                 |                 |                 |                 |
|-------------------------------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed                     | 0 / 262 (0.00%) | 0 / 307 (0.00%) | 1 / 130 (0.77%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 1 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Cholecystitis acute                             |                 |                 |                 |
| subjects affected / exposed                     | 0 / 262 (0.00%) | 0 / 307 (0.00%) | 1 / 130 (0.77%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 1 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Hepatic failure                                 |                 |                 |                 |
| subjects affected / exposed                     | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (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           |
| Hepatic vein thrombosis                         |                 |                 |                 |
| subjects affected / exposed                     | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (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           |
| Hepatitis acute                                 |                 |                 |                 |
| subjects affected / exposed                     | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (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           |
| Portal vein occlusion                           |                 |                 |                 |
| subjects affected / exposed                     | 0 / 262 (0.00%) | 0 / 307 (0.00%) | 1 / 130 (0.77%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Skin and subcutaneous tissue disorders          |                 |                 |                 |
| Dermatitis exfoliative generalised              |                 |                 |                 |
| subjects affected / exposed                     | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (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           |
| Photosensitivity reaction                       |                 |                 |                 |
| subjects affected / exposed                     | 0 / 262 (0.00%) | 0 / 307 (0.00%) | 1 / 130 (0.77%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Rash                                            |                 |                 |                 |

|                                                 |                 |                 |                 |
|-------------------------------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed                     | 0 / 262 (0.00%) | 0 / 307 (0.00%) | 1 / 130 (0.77%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Rash pruritic                                   |                 |                 |                 |
| subjects affected / exposed                     | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (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           |
| Urticaria                                       |                 |                 |                 |
| subjects affected / exposed                     | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (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           |
| Renal and urinary disorders                     |                 |                 |                 |
| Acute kidney injury                             |                 |                 |                 |
| subjects affected / exposed                     | 4 / 262 (1.53%) | 5 / 307 (1.63%) | 3 / 130 (2.31%) |
| occurrences causally related to treatment / all | 1 / 4           | 2 / 5           | 1 / 3           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Renal colic                                     |                 |                 |                 |
| subjects affected / exposed                     | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (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                     | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (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 / 262 (0.00%) | 0 / 307 (0.00%) | 1 / 130 (0.77%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Musculoskeletal and connective tissue disorders |                 |                 |                 |
| Flank pain                                      |                 |                 |                 |
| subjects affected / exposed                     | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (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           |

|                                                 |                  |                  |                 |
|-------------------------------------------------|------------------|------------------|-----------------|
| Pathological fracture                           |                  |                  |                 |
| subjects affected / exposed                     | 1 / 262 (0.38%)  | 0 / 307 (0.00%)  | 0 / 130 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0           |
| Back pain                                       |                  |                  |                 |
| subjects affected / exposed                     | 0 / 262 (0.00%)  | 1 / 307 (0.33%)  | 1 / 130 (0.77%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0           |
| Intervertebral disc protrusion                  |                  |                  |                 |
| subjects affected / exposed                     | 0 / 262 (0.00%)  | 1 / 307 (0.33%)  | 0 / 130 (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           |
| Neck pain                                       |                  |                  |                 |
| subjects affected / exposed                     | 0 / 262 (0.00%)  | 0 / 307 (0.00%)  | 1 / 130 (0.77%) |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 0            | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0           |
| Necrotising myositis                            |                  |                  |                 |
| subjects affected / exposed                     | 0 / 262 (0.00%)  | 1 / 307 (0.33%)  | 0 / 130 (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           |
| Muscular weakness                               |                  |                  |                 |
| subjects affected / exposed                     | 4 / 262 (1.53%)  | 2 / 307 (0.65%)  | 0 / 130 (0.00%) |
| occurrences causally related to treatment / all | 2 / 4            | 1 / 2            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0           |
| Infections and infestations                     |                  |                  |                 |
| COVID-19                                        |                  |                  |                 |
| subjects affected / exposed                     | 13 / 262 (4.96%) | 2 / 307 (0.65%)  | 2 / 130 (1.54%) |
| occurrences causally related to treatment / all | 0 / 13           | 0 / 2            | 0 / 2           |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            | 0 / 0           |
| Pneumonia                                       |                  |                  |                 |
| subjects affected / exposed                     | 11 / 262 (4.20%) | 10 / 307 (3.26%) | 4 / 130 (3.08%) |
| occurrences causally related to treatment / all | 3 / 14           | 6 / 11           | 2 / 5           |
| deaths causally related to treatment / all      | 0 / 0            | 1 / 1            | 1 / 1           |
| COVID-19 pneumonia                              |                  |                  |                 |

|                                                 |                 |                  |                 |
|-------------------------------------------------|-----------------|------------------|-----------------|
| subjects affected / exposed                     | 9 / 262 (3.44%) | 12 / 307 (3.91%) | 2 / 130 (1.54%) |
| occurrences causally related to treatment / all | 2 / 9           | 2 / 12           | 1 / 2           |
| deaths causally related to treatment / all      | 1 / 1           | 0 / 0            | 1 / 1           |
| Sepsis                                          |                 |                  |                 |
| subjects affected / exposed                     | 7 / 262 (2.67%) | 4 / 307 (1.30%)  | 0 / 130 (0.00%) |
| occurrences causally related to treatment / all | 1 / 7           | 6 / 8            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| Septic shock                                    |                 |                  |                 |
| subjects affected / exposed                     | 2 / 262 (0.76%) | 0 / 307 (0.00%)  | 0 / 130 (0.00%) |
| occurrences causally related to treatment / all | 1 / 2           | 0 / 0            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| Urosepsis                                       |                 |                  |                 |
| subjects affected / exposed                     | 2 / 262 (0.76%) | 0 / 307 (0.00%)  | 0 / 130 (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           |
| Appendicitis perforated                         |                 |                  |                 |
| subjects affected / exposed                     | 1 / 262 (0.38%) | 0 / 307 (0.00%)  | 0 / 130 (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           |
| Bacterial infection                             |                 |                  |                 |
| subjects affected / exposed                     | 1 / 262 (0.38%) | 0 / 307 (0.00%)  | 0 / 130 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0            | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0            | 0 / 0           |
| Bronchitis                                      |                 |                  |                 |
| subjects affected / exposed                     | 1 / 262 (0.38%) | 1 / 307 (0.33%)  | 0 / 130 (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           |
| Bronchopulmonary aspergillosis                  |                 |                  |                 |
| subjects affected / exposed                     | 1 / 262 (0.38%) | 0 / 307 (0.00%)  | 0 / 130 (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           |
| Campylobacter infection                         |                 |                  |                 |

|                                                 |                 |                 |                 |
|-------------------------------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed                     | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences causally related to treatment / all | 2 / 2           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Enterocolitis infectious                        |                 |                 |                 |
| subjects affected / exposed                     | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (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           |
| Oesophageal candidiasis                         |                 |                 |                 |
| subjects affected / exposed                     | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (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           |
| Pneumonia bacterial                             |                 |                 |                 |
| subjects affected / exposed                     | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Pneumonia cytomegaloviral                       |                 |                 |                 |
| subjects affected / exposed                     | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (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           |
| Pneumonia haemophilus                           |                 |                 |                 |
| subjects affected / exposed                     | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (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           |
| Pseudomonas infection                           |                 |                 |                 |
| subjects affected / exposed                     | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (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           |
| Urinary tract infection                         |                 |                 |                 |
| subjects affected / exposed                     | 1 / 262 (0.38%) | 3 / 307 (0.98%) | 1 / 130 (0.77%) |
| occurrences causally related to treatment / all | 1 / 1           | 1 / 3           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Anal abscess                                    |                 |                 |                 |

|                                                 |                 |                 |                 |
|-------------------------------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed                     | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (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           |
| Appendicitis                                    |                 |                 |                 |
| subjects affected / exposed                     | 0 / 262 (0.00%) | 0 / 307 (0.00%) | 1 / 130 (0.77%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Bronchitis pneumococcal                         |                 |                 |                 |
| subjects affected / exposed                     | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (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           |
| Cellulitis                                      |                 |                 |                 |
| subjects affected / exposed                     | 0 / 262 (0.00%) | 0 / 307 (0.00%) | 2 / 130 (1.54%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 1 / 2           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Clostridium difficile colitis                   |                 |                 |                 |
| subjects affected / exposed                     | 0 / 262 (0.00%) | 2 / 307 (0.65%) | 2 / 130 (1.54%) |
| occurrences causally related to treatment / all | 0 / 0           | 1 / 2           | 1 / 2           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Clostridium difficile infection                 |                 |                 |                 |
| subjects affected / exposed                     | 0 / 262 (0.00%) | 0 / 307 (0.00%) | 1 / 130 (0.77%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Corneal infection                               |                 |                 |                 |
| subjects affected / exposed                     | 0 / 262 (0.00%) | 0 / 307 (0.00%) | 1 / 130 (0.77%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 1 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Cytomegalovirus infection reactivation          |                 |                 |                 |
| subjects affected / exposed                     | 0 / 262 (0.00%) | 0 / 307 (0.00%) | 2 / 130 (1.54%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 2 / 2           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Empyema                                         |                 |                 |                 |

|                                                 |                 |                 |                 |
|-------------------------------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed                     | 0 / 262 (0.00%) | 0 / 307 (0.00%) | 1 / 130 (0.77%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Escherichia bacteraemia                         |                 |                 |                 |
| subjects affected / exposed                     | 0 / 262 (0.00%) | 0 / 307 (0.00%) | 1 / 130 (0.77%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Gastroenteritis                                 |                 |                 |                 |
| subjects affected / exposed                     | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 1 / 130 (0.77%) |
| occurrences causally related to treatment / all | 0 / 0           | 1 / 1           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Herpes zoster                                   |                 |                 |                 |
| subjects affected / exposed                     | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (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           |
| Influenza                                       |                 |                 |                 |
| subjects affected / exposed                     | 0 / 262 (0.00%) | 0 / 307 (0.00%) | 2 / 130 (1.54%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 1 / 2           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Lower respiratory tract infection               |                 |                 |                 |
| subjects affected / exposed                     | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (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 aseptic                              |                 |                 |                 |
| subjects affected / exposed                     | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (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           |
| Neutropenic sepsis                              |                 |                 |                 |
| subjects affected / exposed                     | 0 / 262 (0.00%) | 0 / 307 (0.00%) | 1 / 130 (0.77%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 1 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Pneumocystis jirovecii pneumonia                |                 |                 |                 |

|                                                 |                 |                 |                 |
|-------------------------------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed                     | 0 / 262 (0.00%) | 0 / 307 (0.00%) | 1 / 130 (0.77%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 1 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Pneumonia legionella                            |                 |                 |                 |
| subjects affected / exposed                     | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (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           |
| Pneumonia serratia                              |                 |                 |                 |
| subjects affected / exposed                     | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Postoperative wound infection                   |                 |                 |                 |
| subjects affected / exposed                     | 0 / 262 (0.00%) | 0 / 307 (0.00%) | 1 / 130 (0.77%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Soft tissue infection                           |                 |                 |                 |
| subjects affected / exposed                     | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (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           |
| Streptococcal sepsis                            |                 |                 |                 |
| subjects affected / exposed                     | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (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           |
| Viral infection                                 |                 |                 |                 |
| subjects affected / exposed                     | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (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           |
| Metabolism and nutrition disorders              |                 |                 |                 |
| Tumour lysis syndrome                           |                 |                 |                 |
| subjects affected / exposed                     | 2 / 262 (0.76%) | 0 / 307 (0.00%) | 1 / 130 (0.77%) |
| occurrences causally related to treatment / all | 2 / 2           | 0 / 0           | 1 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Dehydration                                     |                 |                 |                 |

|                                                 |                 |                 |                 |
|-------------------------------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed                     | 1 / 262 (0.38%) | 5 / 307 (1.63%) | 1 / 130 (0.77%) |
| occurrences causally related to treatment / all | 0 / 1           | 2 / 5           | 1 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Diabetes mellitus                               |                 |                 |                 |
| subjects affected / exposed                     | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (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                     | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (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           |
| Fluid overload                                  |                 |                 |                 |
| subjects affected / exposed                     | 1 / 262 (0.38%) | 1 / 307 (0.33%) | 0 / 130 (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           |
| Hypercalcaemia                                  |                 |                 |                 |
| subjects affected / exposed                     | 1 / 262 (0.38%) | 2 / 307 (0.65%) | 0 / 130 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 2           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Hypokalaemia                                    |                 |                 |                 |
| subjects affected / exposed                     | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 2 / 130 (1.54%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 0           | 1 / 2           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Hyponatraemia                                   |                 |                 |                 |
| subjects affected / exposed                     | 1 / 262 (0.38%) | 1 / 307 (0.33%) | 0 / 130 (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           |
| Tetany                                          |                 |                 |                 |
| subjects affected / exposed                     | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences causally related to treatment / all | 2 / 2           | 0 / 0           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Cachexia                                        |                 |                 |                 |

|                                                 |                 |                 |                 |
|-------------------------------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed                     | 0 / 262 (0.00%) | 0 / 307 (0.00%) | 1 / 130 (0.77%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Hypocalcaemia                                   |                 |                 |                 |
| subjects affected / exposed                     | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (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           |
| Hypophosphataemia                               |                 |                 |                 |
| subjects affected / exposed                     | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 1 / 1           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |

| <b>Serious adverse events</b>                                       | Arm D: Ublituximab Monotherapy | Arm E: Ublituximab to Umbralisib (TGR-1202) |  |
|---------------------------------------------------------------------|--------------------------------|---------------------------------------------|--|
| Total subjects affected by serious adverse events                   |                                |                                             |  |
| subjects affected / exposed                                         | 5 / 24 (20.83%)                | 5 / 12 (41.67%)                             |  |
| number of deaths (all causes)                                       | 2                              | 2                                           |  |
| number of deaths resulting from adverse events                      | 1                              | 0                                           |  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                                |                                             |  |
| Adenocarcinoma pancreas                                             |                                |                                             |  |
| subjects affected / exposed                                         | 0 / 24 (0.00%)                 | 0 / 12 (0.00%)                              |  |
| occurrences causally related to treatment / all                     | 0 / 0                          | 0 / 0                                       |  |
| deaths causally related to treatment / all                          | 0 / 0                          | 0 / 0                                       |  |
| Breast cancer recurrent                                             |                                |                                             |  |
| subjects affected / exposed                                         | 0 / 24 (0.00%)                 | 0 / 12 (0.00%)                              |  |
| occurrences causally related to treatment / all                     | 0 / 0                          | 0 / 0                                       |  |
| deaths causally related to treatment / all                          | 0 / 0                          | 0 / 0                                       |  |
| Gastrointestinal adenocarcinoma                                     |                                |                                             |  |
| subjects affected / exposed                                         | 0 / 24 (0.00%)                 | 0 / 12 (0.00%)                              |  |
| occurrences causally related to treatment / all                     | 0 / 0                          | 0 / 0                                       |  |
| deaths causally related to treatment / all                          | 0 / 0                          | 0 / 0                                       |  |
| Infected neoplasm                                                   |                                |                                             |  |

|                                                      |                |                |  |
|------------------------------------------------------|----------------|----------------|--|
| subjects affected / exposed                          | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          |  |
| Intraductal proliferative breast lesion              |                |                |  |
| subjects affected / exposed                          | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          |  |
| Invasive ductal breast carcinoma                     |                |                |  |
| subjects affected / exposed                          | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          |  |
| Neuroendocrine carcinoma of the skin                 |                |                |  |
| subjects affected / exposed                          | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          |  |
| Anal cancer                                          |                |                |  |
| subjects affected / exposed                          | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          |  |
| Extranodal marginal zone B-cell lymphoma (MALT type) |                |                |  |
| subjects affected / exposed                          | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          |  |
| Gastrointestinal neoplasm                            |                |                |  |
| subjects affected / exposed                          | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          |  |
| Glioma                                               |                |                |  |
| subjects affected / exposed                          | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          |  |
| Lymphoma                                             |                |                |  |

|                                                  |                |                |  |
|--------------------------------------------------|----------------|----------------|--|
| subjects affected / exposed                      | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all  | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all       | 0 / 0          | 0 / 0          |  |
| Malignant melanoma in situ                       |                |                |  |
| subjects affected / exposed                      | 1 / 24 (4.17%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all  | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all       | 0 / 0          | 0 / 0          |  |
| Myelodysplastic syndrome                         |                |                |  |
| subjects affected / exposed                      | 0 / 24 (0.00%) | 0 / 12 (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 / 24 (0.00%) | 0 / 12 (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 of lung                  |                |                |  |
| subjects affected / exposed                      | 0 / 24 (0.00%) | 0 / 12 (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 of skin                  |                |                |  |
| subjects affected / exposed                      | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all  | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all       | 0 / 0          | 0 / 0          |  |
| Superficial spreading melanoma stage unspecified |                |                |  |
| subjects affected / exposed                      | 0 / 24 (0.00%) | 1 / 12 (8.33%) |  |
| occurrences causally related to treatment / all  | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all       | 0 / 0          | 0 / 0          |  |
| Vascular disorders                               |                |                |  |
| Hypotension                                      |                |                |  |
| subjects affected / exposed                      | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all  | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all       | 0 / 0          | 0 / 0          |  |
| Deep vein thrombosis                             |                |                |  |

|                                                 |                |                |  |
|-------------------------------------------------|----------------|----------------|--|
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Embolism                                        |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Circulatory collapse                            |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Orthostatic hypotension                         |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Peripheral ischaemia                            |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Surgical and medical procedures                 |                |                |  |
| Alcohol detoxification                          |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Catheter placement                              |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Fluid replacement                               |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Hip arthroplasty                                |                |                |  |

|                                                      |                |                |  |
|------------------------------------------------------|----------------|----------------|--|
| subjects affected / exposed                          | 0 / 24 (0.00%) | 0 / 12 (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 |                |                |  |
| Chest pain                                           |                |                |  |
| subjects affected / exposed                          | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          |  |
| Death                                                |                |                |  |
| subjects affected / exposed                          | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          |  |
| Fatigue                                              |                |                |  |
| subjects affected / exposed                          | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          |  |
| Incarcerated hernia                                  |                |                |  |
| subjects affected / exposed                          | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          |  |
| Multiple organ dysfunction syndrome                  |                |                |  |
| subjects affected / exposed                          | 0 / 24 (0.00%) | 0 / 12 (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 / 24 (0.00%) | 0 / 12 (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 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          |  |
| Asthenia                                             |                |                |  |

|                                                 |                |                |  |
|-------------------------------------------------|----------------|----------------|--|
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Hypothermia                                     |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (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 / 24 (0.00%) | 0 / 12 (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        |                |                |  |
| Vaginal fistula                                 |                |                |  |
| subjects affected / exposed <sup>[1]</sup>      | 0 / 8 (0.00%)  | 0 / 4 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Penile pain                                     |                |                |  |
| subjects affected / exposed <sup>[2]</sup>      | 0 / 16 (0.00%) | 0 / 8 (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 |                |                |  |
| Dyspnoea                                        |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (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 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Chronic obstructive pulmonary disease           |                |                |  |

|                                                 |                |                |  |
|-------------------------------------------------|----------------|----------------|--|
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (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 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Pleural effusion                                |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Pneumonia aspiration                            |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (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 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Pulmonary congestion                            |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Pulmonary oedema                                |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Acute respiratory distress syndrome             |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Acute respiratory failure                       |                |                |  |

|                                                 |                |                |  |
|-------------------------------------------------|----------------|----------------|--|
| subjects affected / exposed                     | 1 / 24 (4.17%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Cough                                           |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Epistaxis                                       |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Interstitial lung disease                       |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (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 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Psychiatric disorders                           |                |                |  |
| Confusional state                               |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Bipolar disorder                                |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Mental status changes                           |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Investigations                                  |                |                |  |

|                                                 |                |                |  |
|-------------------------------------------------|----------------|----------------|--|
| Alanine aminotransferase increased              |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (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 / 24 (0.00%) | 0 / 12 (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 / 24 (0.00%) | 0 / 12 (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 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Transaminases increased                         |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Blood creatinine increased                      |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Neutrophil count decreased                      |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (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  |                |                |  |
| Infusion related reaction                       |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (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 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Arterial injury                                 |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Hip fracture                                    |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Alcohol poisoning                               |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Arthropod bite                                  |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 1 / 12 (8.33%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Brain contusion                                 |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Contusion                                       |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Femur fracture                                  |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (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 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Overdose                                        |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Pelvic fracture                                 |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Spinal compression fracture                     |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Spinal fracture                                 |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Splenic rupture                                 |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Cardiac disorders                               |                |                |  |
| Cardiac failure                                 |                |                |  |
| subjects affected / exposed                     | 1 / 24 (4.17%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Cardiac arrest                                  |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (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 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Cardio-respiratory arrest                       |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Acute left ventricular failure                  |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Acute myocardial infarction                     |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Aortic valve disease                            |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (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 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Cardiopulmonary failure                         |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Tachycardia                                     |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Ventricular failure                             |                |                |  |

|                                                 |                |                |  |
|-------------------------------------------------|----------------|----------------|--|
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Acute coronary syndrome                         |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Atrial flutter                                  |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Cardiac tamponade                               |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Coronary artery disease                         |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (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 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Pericardial effusion                            |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Stress cardiomyopathy                           |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Supraventricular tachycardia                    |                |                |  |

|                                                 |                |                |  |
|-------------------------------------------------|----------------|----------------|--|
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (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                        |                |                |  |
| Seizure                                         |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Cerebrovascular accident                        |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Headache                                        |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Hyporeflexia                                    |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Lethargy                                        |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Dementia                                        |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Encephalopathy                                  |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Presyncope                                      |                |                |  |

|                                                 |                |                |  |
|-------------------------------------------------|----------------|----------------|--|
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Syncope                                         |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Transient ischaemic attack                      |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Blood and lymphatic system disorders            |                |                |  |
| Febrile neutropenia                             |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Thrombocytopenia                                |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Anaemia                                         |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Lymphadenopathy                                 |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Neutropenia                                     |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Pancytopenia                                    |                |                |  |

|                                                 |                |                |  |
|-------------------------------------------------|----------------|----------------|--|
| subjects affected / exposed                     | 0 / 24 (0.00%) | 1 / 12 (8.33%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Agranulocytosis                                 |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Autoimmune haemolytic anaemia                   |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Haemolytic anaemia                              |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Eye disorders                                   |                |                |  |
| Diplopia                                        |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Optic ischaemic neuropathy                      |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Visual impairment                               |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Gastrointestinal disorders                      |                |                |  |
| Colitis                                         |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (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 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Gastrointestinal haemorrhage                    |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Abdominal pain                                  |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Autoimmune colitis                              |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Bezoar                                          |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Dysphagia                                       |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Gastric haemorrhage                             |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Gastric perforation                             |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Gastrointestinal obstruction                    |                |                |  |

|                                                 |                |                |  |
|-------------------------------------------------|----------------|----------------|--|
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (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 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Pancreatitis acute                              |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (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 / 24 (0.00%) | 0 / 12 (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 / 24 (0.00%) | 0 / 12 (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 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Gastric ulcer                                   |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Ileus                                           |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Large intestinal haemorrhage                    |                |                |  |

|                                                 |                |                |  |
|-------------------------------------------------|----------------|----------------|--|
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Nausea                                          |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Oesophageal stenosis                            |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Oesophagitis                                    |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Rectal haemorrhage                              |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Hepatobiliary disorders                         |                |                |  |
| Autoimmune hepatitis                            |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 1 / 12 (8.33%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Cholangitis                                     |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Cholecystitis acute                             |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Hepatic failure                                 |                |                |  |

|                                                 |                |                |  |
|-------------------------------------------------|----------------|----------------|--|
| subjects affected / exposed                     | 1 / 24 (4.17%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 1 / 1          | 0 / 0          |  |
| Hepatic vein thrombosis                         |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Hepatitis acute                                 |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Portal vein occlusion                           |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (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          |                |                |  |
| Dermatitis exfoliative generalised              |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Photosensitivity reaction                       |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (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 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Rash pruritic                                   |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Urticaria                                       |                |                |  |

|                                                 |                |                |  |
|-------------------------------------------------|----------------|----------------|--|
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (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                     | 1 / 24 (4.17%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Renal colic                                     |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (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 / 24 (0.00%) | 0 / 12 (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 / 24 (0.00%) | 0 / 12 (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 |                |                |  |
| Flank pain                                      |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Pathological fracture                           |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (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 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |

|                                                 |                |                |  |
|-------------------------------------------------|----------------|----------------|--|
| Intervertebral disc protrusion                  |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Neck pain                                       |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Necrotising myositis                            |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Muscular weakness                               |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Infections and infestations                     |                |                |  |
| COVID-19                                        |                |                |  |
| subjects affected / exposed                     | 1 / 24 (4.17%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Pneumonia                                       |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| COVID-19 pneumonia                              |                |                |  |
| subjects affected / exposed                     | 1 / 24 (4.17%) | 1 / 12 (8.33%) |  |
| occurrences causally related to treatment / all | 1 / 1          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Sepsis                                          |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Septic shock                                    |                |                |  |

|                                                 |                |                |  |
|-------------------------------------------------|----------------|----------------|--|
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Urosepsis                                       |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Appendicitis perforated                         |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Bacterial infection                             |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Bronchitis                                      |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Bronchopulmonary aspergillosis                  |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Campylobacter infection                         |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Enterocolitis infectious                        |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Oesophageal candidiasis                         |                |                |  |

|                                                 |                |                |  |
|-------------------------------------------------|----------------|----------------|--|
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Pneumonia bacterial                             |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Pneumonia cytomegaloviral                       |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Pneumonia haemophilus                           |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Pseudomonas infection                           |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (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 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Anal abscess                                    |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Appendicitis                                    |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Bronchitis pneumococcal                         |                |                |  |

|                                                 |                |                |  |
|-------------------------------------------------|----------------|----------------|--|
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Cellulitis                                      |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Clostridium difficile colitis                   |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Clostridium difficile infection                 |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Corneal infection                               |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Cytomegalovirus infection reactivation          |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Empyema                                         |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Escherichia bacteraemia                         |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Gastroenteritis                                 |                |                |  |

|                                                 |                |                |  |
|-------------------------------------------------|----------------|----------------|--|
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Herpes zoster                                   |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Influenza                                       |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Lower respiratory tract infection               |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Meningitis aseptic                              |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Neutropenic sepsis                              |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Pneumocystis jirovecii pneumonia                |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Pneumonia legionella                            |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Pneumonia serratia                              |                |                |  |

|                                                 |                |                |  |
|-------------------------------------------------|----------------|----------------|--|
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Postoperative wound infection                   |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Soft tissue infection                           |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Streptococcal sepsis                            |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Viral infection                                 |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (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              |                |                |  |
| Tumour lysis syndrome                           |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Dehydration                                     |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Diabetes mellitus                               |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Failure to thrive                               |                |                |  |

|                                                 |                |                |  |
|-------------------------------------------------|----------------|----------------|--|
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Fluid overload                                  |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Hypercalcaemia                                  |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (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 / 24 (0.00%) | 0 / 12 (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 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Tetany                                          |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Cachexia                                        |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Hypocalcaemia                                   |                |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Hypophosphataemia                               |                |                |  |

|                                                 |                |                |  |
|-------------------------------------------------|----------------|----------------|--|
| subjects affected / exposed                     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.

Justification: Number of subjects exposed to this adverse event term is based on the female population in this study.

[2] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.

Justification: Number of subjects exposed to this adverse event term is based on the male population in this study.

Frequency threshold for reporting non-serious adverse events: 0 %

| <b>Non-serious adverse events</b>                                   | Arm A: Ublituximab + Umbralisib (TGR-1202) | Arm B: Umbralisib (TGR-1202) Monotherapy | Arm C: Ublituximab + Umbralisib (TGR-1202) + Bendamustine |
|---------------------------------------------------------------------|--------------------------------------------|------------------------------------------|-----------------------------------------------------------|
| Total subjects affected by non-serious adverse events               |                                            |                                          |                                                           |
| subjects affected / exposed                                         | 254 / 262 (96.95%)                         | 303 / 307 (98.70%)                       | 125 / 130 (96.15%)                                        |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                                            |                                          |                                                           |
| Basal cell carcinoma                                                |                                            |                                          |                                                           |
| subjects affected / exposed                                         | 5 / 262 (1.91%)                            | 1 / 307 (0.33%)                          | 0 / 130 (0.00%)                                           |
| occurrences (all)                                                   | 6                                          | 1                                        | 0                                                         |
| Lipoma                                                              |                                            |                                          |                                                           |
| subjects affected / exposed                                         | 2 / 262 (0.76%)                            | 2 / 307 (0.65%)                          | 0 / 130 (0.00%)                                           |
| occurrences (all)                                                   | 2                                          | 2                                        | 0                                                         |
| Benign neoplasm of eye                                              |                                            |                                          |                                                           |
| subjects affected / exposed                                         | 1 / 262 (0.38%)                            | 0 / 307 (0.00%)                          | 0 / 130 (0.00%)                                           |
| occurrences (all)                                                   | 1                                          | 0                                        | 0                                                         |
| Bowen's disease                                                     |                                            |                                          |                                                           |
| subjects affected / exposed                                         | 1 / 262 (0.38%)                            | 0 / 307 (0.00%)                          | 0 / 130 (0.00%)                                           |
| occurrences (all)                                                   | 1                                          | 0                                        | 0                                                         |
| Central nervous system lymphoma                                     |                                            |                                          |                                                           |
| subjects affected / exposed                                         | 1 / 262 (0.38%)                            | 0 / 307 (0.00%)                          | 0 / 130 (0.00%)                                           |
| occurrences (all)                                                   | 1                                          | 0                                        | 0                                                         |
| Haemangioma of skin                                                 |                                            |                                          |                                                           |
| subjects affected / exposed                                         | 1 / 262 (0.38%)                            | 0 / 307 (0.00%)                          | 0 / 130 (0.00%)                                           |
| occurrences (all)                                                   | 1                                          | 0                                        | 0                                                         |
| Meningioma                                                          |                                            |                                          |                                                           |

|                                          |                 |                 |                 |
|------------------------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed              | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)                        | 1               | 0               | 0               |
| Neoplasm skin                            |                 |                 |                 |
| subjects affected / exposed              | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)                        | 1               | 0               | 0               |
| Seborrhoeic keratosis                    |                 |                 |                 |
| subjects affected / exposed              | 1 / 262 (0.38%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)                        | 1               | 1               | 0               |
| Skin cancer                              |                 |                 |                 |
| subjects affected / exposed              | 1 / 262 (0.38%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)                        | 1               | 1               | 0               |
| Squamous cell carcinoma of head and neck |                 |                 |                 |
| subjects affected / exposed              | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 1 / 130 (0.77%) |
| occurrences (all)                        | 1               | 0               | 1               |
| Tumour pain                              |                 |                 |                 |
| subjects affected / exposed              | 1 / 262 (0.38%) | 4 / 307 (1.30%) | 3 / 130 (2.31%) |
| occurrences (all)                        | 1               | 4               | 4               |
| Cancer pain                              |                 |                 |                 |
| subjects affected / exposed              | 0 / 262 (0.00%) | 0 / 307 (0.00%) | 2 / 130 (1.54%) |
| occurrences (all)                        | 0               | 0               | 2               |
| Gastrointestinal tract adenoma           |                 |                 |                 |
| subjects affected / exposed              | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)                        | 0               | 1               | 0               |
| Haemangioma                              |                 |                 |                 |
| subjects affected / exposed              | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)                        | 0               | 1               | 0               |
| Neoplasm                                 |                 |                 |                 |
| subjects affected / exposed              | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)                        | 0               | 1               | 0               |
| Oral neoplasm                            |                 |                 |                 |
| subjects affected / exposed              | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)                        | 0               | 1               | 0               |
| Skin neoplasm bleeding                   |                 |                 |                 |
| subjects affected / exposed              | 0 / 262 (0.00%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)                        | 0               | 0               | 0               |

|                                                                                     |                        |                        |                         |
|-------------------------------------------------------------------------------------|------------------------|------------------------|-------------------------|
| Squamous cell carcinoma<br>subjects affected / exposed<br>occurrences (all)         | 0 / 262 (0.00%)<br>0   | 1 / 307 (0.33%)<br>1   | 0 / 130 (0.00%)<br>0    |
| Squamous cell carcinoma of skin<br>subjects affected / exposed<br>occurrences (all) | 0 / 262 (0.00%)<br>0   | 1 / 307 (0.33%)<br>1   | 0 / 130 (0.00%)<br>0    |
| Vascular disorders                                                                  |                        |                        |                         |
| Hypertension<br>subjects affected / exposed<br>occurrences (all)                    | 20 / 262 (7.63%)<br>29 | 23 / 307 (7.49%)<br>34 | 2 / 130 (1.54%)<br>2    |
| Flushing<br>subjects affected / exposed<br>occurrences (all)                        | 10 / 262 (3.82%)<br>11 | 4 / 307 (1.30%)<br>4   | 2 / 130 (1.54%)<br>2    |
| Hypotension<br>subjects affected / exposed<br>occurrences (all)                     | 7 / 262 (2.67%)<br>7   | 10 / 307 (3.26%)<br>12 | 13 / 130 (10.00%)<br>19 |
| Hot flush<br>subjects affected / exposed<br>occurrences (all)                       | 5 / 262 (1.91%)<br>5   | 18 / 307 (5.86%)<br>19 | 1 / 130 (0.77%)<br>1    |
| Deep vein thrombosis<br>subjects affected / exposed<br>occurrences (all)            | 2 / 262 (0.76%)<br>2   | 2 / 307 (0.65%)<br>2   | 2 / 130 (1.54%)<br>2    |
| Haematoma<br>subjects affected / exposed<br>occurrences (all)                       | 1 / 262 (0.38%)<br>2   | 2 / 307 (0.65%)<br>2   | 0 / 130 (0.00%)<br>0    |
| Lymphoedema<br>subjects affected / exposed<br>occurrences (all)                     | 1 / 262 (0.38%)<br>1   | 0 / 307 (0.00%)<br>0   | 0 / 130 (0.00%)<br>0    |
| Thrombophlebitis superficial<br>subjects affected / exposed<br>occurrences (all)    | 1 / 262 (0.38%)<br>1   | 0 / 307 (0.00%)<br>0   | 2 / 130 (1.54%)<br>2    |
| Arterial thrombosis<br>subjects affected / exposed<br>occurrences (all)             | 0 / 262 (0.00%)<br>0   | 1 / 307 (0.33%)<br>1   | 0 / 130 (0.00%)<br>0    |
| Embolism                                                                            |                        |                        |                         |

|                                 |                 |                 |                 |
|---------------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed     | 0 / 262 (0.00%) | 3 / 307 (0.98%) | 1 / 130 (0.77%) |
| occurrences (all)               | 0               | 3               | 1               |
| Embolism venous                 |                 |                 |                 |
| subjects affected / exposed     | 0 / 262 (0.00%) | 0 / 307 (0.00%) | 1 / 130 (0.77%) |
| occurrences (all)               | 0               | 0               | 1               |
| Haemorrhage                     |                 |                 |                 |
| subjects affected / exposed     | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)               | 0               | 1               | 0               |
| Hyperaemia                      |                 |                 |                 |
| subjects affected / exposed     | 0 / 262 (0.00%) | 2 / 307 (0.65%) | 0 / 130 (0.00%) |
| occurrences (all)               | 0               | 2               | 0               |
| Pallor                          |                 |                 |                 |
| subjects affected / exposed     | 0 / 262 (0.00%) | 0 / 307 (0.00%) | 1 / 130 (0.77%) |
| occurrences (all)               | 0               | 0               | 1               |
| Peripheral coldness             |                 |                 |                 |
| subjects affected / exposed     | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)               | 0               | 1               | 0               |
| Peripheral venous disease       |                 |                 |                 |
| subjects affected / exposed     | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)               | 0               | 1               | 0               |
| Subgaleal haematoma             |                 |                 |                 |
| subjects affected / exposed     | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)               | 0               | 1               | 0               |
| Varicose vein                   |                 |                 |                 |
| subjects affected / exposed     | 0 / 262 (0.00%) | 0 / 307 (0.00%) | 1 / 130 (0.77%) |
| occurrences (all)               | 0               | 0               | 1               |
| Vascular insufficiency          |                 |                 |                 |
| subjects affected / exposed     | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)               | 0               | 1               | 0               |
| Vasculitis                      |                 |                 |                 |
| subjects affected / exposed     | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)               | 0               | 1               | 0               |
| Surgical and medical procedures |                 |                 |                 |
| Skin neoplasm excision          |                 |                 |                 |
| subjects affected / exposed     | 2 / 262 (0.76%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)               | 4               | 0               | 0               |

|                                                                        |                          |                          |                         |
|------------------------------------------------------------------------|--------------------------|--------------------------|-------------------------|
| Hip arthroplasty<br>subjects affected / exposed<br>occurrences (all)   | 1 / 262 (0.38%)<br>1     | 0 / 307 (0.00%)<br>0     | 0 / 130 (0.00%)<br>0    |
| Tooth extraction<br>subjects affected / exposed<br>occurrences (all)   | 1 / 262 (0.38%)<br>1     | 2 / 307 (0.65%)<br>2     | 0 / 130 (0.00%)<br>0    |
| Cancer surgery<br>subjects affected / exposed<br>occurrences (all)     | 0 / 262 (0.00%)<br>0     | 0 / 307 (0.00%)<br>0     | 1 / 130 (0.77%)<br>1    |
| Cataract operation<br>subjects affected / exposed<br>occurrences (all) | 0 / 262 (0.00%)<br>0     | 1 / 307 (0.33%)<br>2     | 0 / 130 (0.00%)<br>0    |
| Cerumen removal<br>subjects affected / exposed<br>occurrences (all)    | 0 / 262 (0.00%)<br>0     | 0 / 307 (0.00%)<br>0     | 1 / 130 (0.77%)<br>1    |
| Knee arthroplasty<br>subjects affected / exposed<br>occurrences (all)  | 0 / 262 (0.00%)<br>0     | 1 / 307 (0.33%)<br>2     | 0 / 130 (0.00%)<br>0    |
| General disorders and administration<br>site conditions                |                          |                          |                         |
| Fatigue<br>subjects affected / exposed<br>occurrences (all)            | 80 / 262 (30.53%)<br>109 | 96 / 307 (31.27%)<br>133 | 49 / 130 (37.69%)<br>71 |
| Oedema peripheral<br>subjects affected / exposed<br>occurrences (all)  | 35 / 262 (13.36%)<br>43  | 35 / 307 (11.40%)<br>51  | 15 / 130 (11.54%)<br>19 |
| Pyrexia<br>subjects affected / exposed<br>occurrences (all)            | 32 / 262 (12.21%)<br>37  | 37 / 307 (12.05%)<br>63  | 17 / 130 (13.08%)<br>29 |
| Asthenia<br>subjects affected / exposed<br>occurrences (all)           | 25 / 262 (9.54%)<br>30   | 29 / 307 (9.45%)<br>37   | 14 / 130 (10.77%)<br>20 |
| Chills<br>subjects affected / exposed<br>occurrences (all)             | 23 / 262 (8.78%)<br>32   | 22 / 307 (7.17%)<br>27   | 6 / 130 (4.62%)<br>6    |
| Non-cardiac chest pain                                                 |                          |                          |                         |

|                             |                 |                  |                 |
|-----------------------------|-----------------|------------------|-----------------|
| subjects affected / exposed | 9 / 262 (3.44%) | 5 / 307 (1.63%)  | 1 / 130 (0.77%) |
| occurrences (all)           | 9               | 6                | 1               |
| Pain                        |                 |                  |                 |
| subjects affected / exposed | 9 / 262 (3.44%) | 7 / 307 (2.28%)  | 6 / 130 (4.62%) |
| occurrences (all)           | 9               | 7                | 6               |
| Chest discomfort            |                 |                  |                 |
| subjects affected / exposed | 6 / 262 (2.29%) | 3 / 307 (0.98%)  | 3 / 130 (2.31%) |
| occurrences (all)           | 6               | 4                | 3               |
| Peripheral swelling         |                 |                  |                 |
| subjects affected / exposed | 6 / 262 (2.29%) | 10 / 307 (3.26%) | 4 / 130 (3.08%) |
| occurrences (all)           | 8               | 11               | 4               |
| Feeling abnormal            |                 |                  |                 |
| subjects affected / exposed | 4 / 262 (1.53%) | 3 / 307 (0.98%)  | 0 / 130 (0.00%) |
| occurrences (all)           | 4               | 5                | 0               |
| Influenza like illness      |                 |                  |                 |
| subjects affected / exposed | 4 / 262 (1.53%) | 4 / 307 (1.30%)  | 3 / 130 (2.31%) |
| occurrences (all)           | 5               | 4                | 3               |
| Swelling                    |                 |                  |                 |
| subjects affected / exposed | 4 / 262 (1.53%) | 2 / 307 (0.65%)  | 0 / 130 (0.00%) |
| occurrences (all)           | 4               | 3                | 0               |
| Catheter site pain          |                 |                  |                 |
| subjects affected / exposed | 3 / 262 (1.15%) | 2 / 307 (0.65%)  | 0 / 130 (0.00%) |
| occurrences (all)           | 3               | 2                | 0               |
| Chest pain                  |                 |                  |                 |
| subjects affected / exposed | 3 / 262 (1.15%) | 8 / 307 (2.61%)  | 2 / 130 (1.54%) |
| occurrences (all)           | 3               | 8                | 3               |
| Face oedema                 |                 |                  |                 |
| subjects affected / exposed | 2 / 262 (0.76%) | 2 / 307 (0.65%)  | 2 / 130 (1.54%) |
| occurrences (all)           | 2               | 2                | 2               |
| Feeling hot                 |                 |                  |                 |
| subjects affected / exposed | 2 / 262 (0.76%) | 0 / 307 (0.00%)  | 0 / 130 (0.00%) |
| occurrences (all)           | 2               | 0                | 0               |
| Gait disturbance            |                 |                  |                 |
| subjects affected / exposed | 2 / 262 (0.76%) | 3 / 307 (0.98%)  | 2 / 130 (1.54%) |
| occurrences (all)           | 2               | 3                | 2               |
| Localised oedema            |                 |                  |                 |

|                                   |                 |                 |                 |
|-----------------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed       | 2 / 262 (0.76%) | 3 / 307 (0.98%) | 1 / 130 (0.77%) |
| occurrences (all)                 | 2               | 3               | 1               |
| Malaise                           |                 |                 |                 |
| subjects affected / exposed       | 2 / 262 (0.76%) | 7 / 307 (2.28%) | 0 / 130 (0.00%) |
| occurrences (all)                 | 3               | 8               | 0               |
| Swelling face                     |                 |                 |                 |
| subjects affected / exposed       | 2 / 262 (0.76%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)                 | 2               | 0               | 0               |
| Administration site extravasation |                 |                 |                 |
| subjects affected / exposed       | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)                 | 1               | 0               | 0               |
| Adverse drug reaction             |                 |                 |                 |
| subjects affected / exposed       | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)                 | 1               | 0               | 0               |
| Axillary pain                     |                 |                 |                 |
| subjects affected / exposed       | 1 / 262 (0.38%) | 2 / 307 (0.65%) | 0 / 130 (0.00%) |
| occurrences (all)                 | 1               | 2               | 0               |
| Catheter site swelling            |                 |                 |                 |
| subjects affected / exposed       | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)                 | 1               | 0               | 0               |
| Discomfort                        |                 |                 |                 |
| subjects affected / exposed       | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 1 / 130 (0.77%) |
| occurrences (all)                 | 1               | 0               | 1               |
| Early satiety                     |                 |                 |                 |
| subjects affected / exposed       | 1 / 262 (0.38%) | 1 / 307 (0.33%) | 1 / 130 (0.77%) |
| occurrences (all)                 | 1               | 1               | 1               |
| Facial pain                       |                 |                 |                 |
| subjects affected / exposed       | 1 / 262 (0.38%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)                 | 1               | 2               | 0               |
| Feeling jittery                   |                 |                 |                 |
| subjects affected / exposed       | 1 / 262 (0.38%) | 1 / 307 (0.33%) | 1 / 130 (0.77%) |
| occurrences (all)                 | 1               | 2               | 1               |
| Illness                           |                 |                 |                 |
| subjects affected / exposed       | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)                 | 1               | 0               | 0               |
| Injection site bruising           |                 |                 |                 |

|                                       |                 |                 |                 |
|---------------------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed           | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)                     | 1               | 0               | 0               |
| Mucosal inflammation                  |                 |                 |                 |
| subjects affected / exposed           | 1 / 262 (0.38%) | 2 / 307 (0.65%) | 1 / 130 (0.77%) |
| occurrences (all)                     | 1               | 2               | 1               |
| Oedema                                |                 |                 |                 |
| subjects affected / exposed           | 1 / 262 (0.38%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)                     | 1               | 1               | 0               |
| Performance status decreased          |                 |                 |                 |
| subjects affected / exposed           | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)                     | 1               | 0               | 0               |
| Disease progression                   |                 |                 |                 |
| subjects affected / exposed           | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)                     | 0               | 1               | 0               |
| Drug intolerance                      |                 |                 |                 |
| subjects affected / exposed           | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)                     | 0               | 1               | 0               |
| Exercise tolerance decreased          |                 |                 |                 |
| subjects affected / exposed           | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)                     | 0               | 1               | 0               |
| Feeling cold                          |                 |                 |                 |
| subjects affected / exposed           | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)                     | 1               | 0               | 0               |
| General physical health deterioration |                 |                 |                 |
| subjects affected / exposed           | 0 / 262 (0.00%) | 0 / 307 (0.00%) | 1 / 130 (0.77%) |
| occurrences (all)                     | 0               | 0               | 1               |
| Generalised oedema                    |                 |                 |                 |
| subjects affected / exposed           | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)                     | 0               | 1               | 0               |
| Mass                                  |                 |                 |                 |
| subjects affected / exposed           | 0 / 262 (0.00%) | 0 / 307 (0.00%) | 1 / 130 (0.77%) |
| occurrences (all)                     | 0               | 0               | 1               |
| Mucosal hyperaemia                    |                 |                 |                 |
| subjects affected / exposed           | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)                     | 0               | 1               | 0               |
| Nodule                                |                 |                 |                 |

|                             |                 |                 |                 |
|-----------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 262 (0.00%) | 2 / 307 (0.65%) | 0 / 130 (0.00%) |
| occurrences (all)           | 0               | 2               | 0               |
| Sensation of foreign body   |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)           | 0               | 1               | 0               |
| Temperature intolerance     |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 2 / 307 (0.65%) | 0 / 130 (0.00%) |
| occurrences (all)           | 0               | 2               | 0               |
| Tenderness                  |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 0 / 307 (0.00%) | 1 / 130 (0.77%) |
| occurrences (all)           | 0               | 0               | 1               |
| Thirst                      |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 1 / 130 (0.77%) |
| occurrences (all)           | 0               | 1               | 1               |
| Tissue infiltration         |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 0 / 307 (0.00%) | 1 / 130 (0.77%) |
| occurrences (all)           | 0               | 0               | 1               |
| Immune system disorders     |                 |                 |                 |
| Hypersensitivity            |                 |                 |                 |
| subjects affected / exposed | 5 / 262 (1.91%) | 0 / 307 (0.00%) | 1 / 130 (0.77%) |
| occurrences (all)           | 6               | 0               | 2               |
| Seasonal allergy            |                 |                 |                 |
| subjects affected / exposed | 3 / 262 (1.15%) | 3 / 307 (0.98%) | 0 / 130 (0.00%) |
| occurrences (all)           | 3               | 3               | 0               |
| Drug hypersensitivity       |                 |                 |                 |
| subjects affected / exposed | 2 / 262 (0.76%) | 2 / 307 (0.65%) | 0 / 130 (0.00%) |
| occurrences (all)           | 4               | 4               | 0               |
| Hypogammaglobulinaemia      |                 |                 |                 |
| subjects affected / exposed | 2 / 262 (0.76%) | 2 / 307 (0.65%) | 1 / 130 (0.77%) |
| occurrences (all)           | 2               | 2               | 1               |
| Allergy to animal           |                 |                 |                 |
| subjects affected / exposed | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)           | 1               | 0               | 0               |
| Contrast media allergy      |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)           | 0               | 1               | 0               |

|                                                                                                 |                      |                      |                      |
|-------------------------------------------------------------------------------------------------|----------------------|----------------------|----------------------|
| Contrast media reaction<br>subjects affected / exposed<br>occurrences (all)                     | 0 / 262 (0.00%)<br>0 | 1 / 307 (0.33%)<br>1 | 0 / 130 (0.00%)<br>0 |
| Immunodeficiency<br>subjects affected / exposed<br>occurrences (all)                            | 0 / 262 (0.00%)<br>0 | 1 / 307 (0.33%)<br>1 | 0 / 130 (0.00%)<br>0 |
| Sarcoidosis<br>subjects affected / exposed<br>occurrences (all)                                 | 0 / 262 (0.00%)<br>0 | 1 / 307 (0.33%)<br>1 | 0 / 130 (0.00%)<br>0 |
| Reproductive system and breast disorders                                                        |                      |                      |                      |
| Scrotal oedema<br>subjects affected / exposed <sup>[3]</sup><br>occurrences (all)               | 2 / 157 (1.27%)<br>2 | 0 / 168 (0.00%)<br>0 | 0 / 78 (0.00%)<br>0  |
| Oedema genital<br>subjects affected / exposed<br>occurrences (all)                              | 1 / 262 (0.38%)<br>1 | 0 / 307 (0.00%)<br>0 | 0 / 130 (0.00%)<br>0 |
| Pelvic pain<br>subjects affected / exposed<br>occurrences (all)                                 | 1 / 262 (0.38%)<br>1 | 0 / 307 (0.00%)<br>0 | 0 / 130 (0.00%)<br>0 |
| Vulvovaginal pain<br>subjects affected / exposed <sup>[4]</sup><br>occurrences (all)            | 1 / 105 (0.95%)<br>2 | 0 / 139 (0.00%)<br>0 | 0 / 52 (0.00%)<br>0  |
| Benign prostatic hyperplasia<br>subjects affected / exposed <sup>[5]</sup><br>occurrences (all) | 0 / 157 (0.00%)<br>0 | 2 / 168 (1.19%)<br>2 | 1 / 78 (1.28%)<br>1  |
| Breast discolouration<br>subjects affected / exposed <sup>[6]</sup><br>occurrences (all)        | 0 / 105 (0.00%)<br>0 | 1 / 139 (0.72%)<br>1 | 0 / 52 (0.00%)<br>0  |
| Breast mass<br>subjects affected / exposed <sup>[7]</sup><br>occurrences (all)                  | 0 / 105 (0.00%)<br>0 | 0 / 139 (0.00%)<br>0 | 1 / 52 (1.92%)<br>1  |
| Breast oedema<br>subjects affected / exposed <sup>[8]</sup><br>occurrences (all)                | 0 / 105 (0.00%)<br>0 | 1 / 139 (0.72%)<br>1 | 0 / 52 (0.00%)<br>0  |
| Breast pain                                                                                     |                      |                      |                      |

|                                             |                 |                 |                 |
|---------------------------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed <sup>[9]</sup>  | 0 / 105 (0.00%) | 2 / 139 (1.44%) | 1 / 52 (1.92%)  |
| occurrences (all)                           | 0               | 2               | 1               |
| Breast swelling                             |                 |                 |                 |
| subjects affected / exposed <sup>[10]</sup> | 0 / 105 (0.00%) | 1 / 139 (0.72%) | 0 / 52 (0.00%)  |
| occurrences (all)                           | 0               | 1               | 0               |
| Genital lesion                              |                 |                 |                 |
| subjects affected / exposed                 | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)                           | 0               | 1               | 0               |
| Genital rash                                |                 |                 |                 |
| subjects affected / exposed                 | 0 / 262 (0.00%) | 2 / 307 (0.65%) | 0 / 130 (0.00%) |
| occurrences (all)                           | 0               | 2               | 0               |
| Gynaecomastia                               |                 |                 |                 |
| subjects affected / exposed <sup>[11]</sup> | 0 / 105 (0.00%) | 1 / 139 (0.72%) | 0 / 52 (0.00%)  |
| occurrences (all)                           | 0               | 1               | 0               |
| Menstruation irregular                      |                 |                 |                 |
| subjects affected / exposed <sup>[12]</sup> | 0 / 105 (0.00%) | 0 / 139 (0.00%) | 0 / 52 (0.00%)  |
| occurrences (all)                           | 0               | 0               | 0               |
| Orchitis noninfective                       |                 |                 |                 |
| subjects affected / exposed <sup>[13]</sup> | 0 / 157 (0.00%) | 1 / 168 (0.60%) | 0 / 78 (0.00%)  |
| occurrences (all)                           | 0               | 1               | 0               |
| Peyronie's disease                          |                 |                 |                 |
| subjects affected / exposed <sup>[14]</sup> | 0 / 157 (0.00%) | 0 / 168 (0.00%) | 1 / 78 (1.28%)  |
| occurrences (all)                           | 0               | 0               | 1               |
| Testicular oedema                           |                 |                 |                 |
| subjects affected / exposed <sup>[15]</sup> | 0 / 157 (0.00%) | 1 / 168 (0.60%) | 0 / 78 (0.00%)  |
| occurrences (all)                           | 0               | 1               | 0               |
| Testicular pain                             |                 |                 |                 |
| subjects affected / exposed <sup>[16]</sup> | 0 / 157 (0.00%) | 1 / 168 (0.60%) | 1 / 78 (1.28%)  |
| occurrences (all)                           | 0               | 1               | 1               |
| Vaginal haemorrhage                         |                 |                 |                 |
| subjects affected / exposed <sup>[17]</sup> | 0 / 105 (0.00%) | 0 / 139 (0.00%) | 2 / 52 (3.85%)  |
| occurrences (all)                           | 0               | 0               | 2               |
| Vulvovaginal dryness                        |                 |                 |                 |
| subjects affected / exposed <sup>[18]</sup> | 0 / 105 (0.00%) | 0 / 139 (0.00%) | 1 / 52 (1.92%)  |
| occurrences (all)                           | 0               | 0               | 1               |
| Vulvovaginal pruritus                       |                 |                 |                 |

|                                                                  |                      |                      |                     |
|------------------------------------------------------------------|----------------------|----------------------|---------------------|
| subjects affected / exposed <sup>[19]</sup><br>occurrences (all) | 0 / 105 (0.00%)<br>0 | 0 / 139 (0.00%)<br>0 | 1 / 52 (1.92%)<br>1 |
| Respiratory, thoracic and mediastinal disorders                  |                      |                      |                     |
| Dyspnoea                                                         |                      |                      |                     |
| subjects affected / exposed                                      | 41 / 262 (15.65%)    | 33 / 307 (10.75%)    | 18 / 130 (13.85%)   |
| occurrences (all)                                                | 48                   | 37                   | 23                  |
| Cough                                                            |                      |                      |                     |
| subjects affected / exposed                                      | 32 / 262 (12.21%)    | 57 / 307 (18.57%)    | 17 / 130 (13.08%)   |
| occurrences (all)                                                | 46                   | 78                   | 26                  |
| Oropharyngeal pain                                               |                      |                      |                     |
| subjects affected / exposed                                      | 10 / 262 (3.82%)     | 13 / 307 (4.23%)     | 5 / 130 (3.85%)     |
| occurrences (all)                                                | 10                   | 13                   | 5                   |
| Pleural effusion                                                 |                      |                      |                     |
| subjects affected / exposed                                      | 7 / 262 (2.67%)      | 11 / 307 (3.58%)     | 2 / 130 (1.54%)     |
| occurrences (all)                                                | 7                    | 13                   | 17                  |
| Productive cough                                                 |                      |                      |                     |
| subjects affected / exposed                                      | 7 / 262 (2.67%)      | 9 / 307 (2.93%)      | 2 / 130 (1.54%)     |
| occurrences (all)                                                | 8                    | 11                   | 2                   |
| Dysphonia                                                        |                      |                      |                     |
| subjects affected / exposed                                      | 6 / 262 (2.29%)      | 4 / 307 (1.30%)      | 1 / 130 (0.77%)     |
| occurrences (all)                                                | 6                    | 4                    | 1                   |
| Nasal congestion                                                 |                      |                      |                     |
| subjects affected / exposed                                      | 5 / 262 (1.91%)      | 9 / 307 (2.93%)      | 3 / 130 (2.31%)     |
| occurrences (all)                                                | 5                    | 11                   | 3                   |
| Chronic obstructive pulmonary disease                            |                      |                      |                     |
| subjects affected / exposed                                      | 4 / 262 (1.53%)      | 0 / 307 (0.00%)      | 3 / 130 (2.31%)     |
| occurrences (all)                                                | 4                    | 0                    | 3                   |
| Epistaxis                                                        |                      |                      |                     |
| subjects affected / exposed                                      | 3 / 262 (1.15%)      | 7 / 307 (2.28%)      | 3 / 130 (2.31%)     |
| occurrences (all)                                                | 7                    | 7                    | 3                   |
| Hypoxia                                                          |                      |                      |                     |
| subjects affected / exposed                                      | 3 / 262 (1.15%)      | 6 / 307 (1.95%)      | 2 / 130 (1.54%)     |
| occurrences (all)                                                | 3                    | 6                    | 2                   |
| Pulmonary oedema                                                 |                      |                      |                     |

|                              |                 |                 |                 |
|------------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed  | 3 / 262 (1.15%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)            | 3               | 1               | 0               |
| Respiratory tract congestion |                 |                 |                 |
| subjects affected / exposed  | 3 / 262 (1.15%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)            | 3               | 0               | 0               |
| Rhinitis allergic            |                 |                 |                 |
| subjects affected / exposed  | 3 / 262 (1.15%) | 4 / 307 (1.30%) | 3 / 130 (2.31%) |
| occurrences (all)            | 3               | 5               | 3               |
| Upper-airway cough syndrome  |                 |                 |                 |
| subjects affected / exposed  | 3 / 262 (1.15%) | 5 / 307 (1.63%) | 2 / 130 (1.54%) |
| occurrences (all)            | 3               | 5               | 2               |
| Wheezing                     |                 |                 |                 |
| subjects affected / exposed  | 3 / 262 (1.15%) | 4 / 307 (1.30%) | 0 / 130 (0.00%) |
| occurrences (all)            | 3               | 4               | 0               |
| Dyspnoea exertional          |                 |                 |                 |
| subjects affected / exposed  | 2 / 262 (0.76%) | 6 / 307 (1.95%) | 4 / 130 (3.08%) |
| occurrences (all)            | 2               | 6               | 6               |
| Haemoptysis                  |                 |                 |                 |
| subjects affected / exposed  | 2 / 262 (0.76%) | 3 / 307 (0.98%) | 1 / 130 (0.77%) |
| occurrences (all)            | 2               | 3               | 1               |
| Hiccups                      |                 |                 |                 |
| subjects affected / exposed  | 2 / 262 (0.76%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)            | 2               | 1               | 0               |
| Rhinorrhoea                  |                 |                 |                 |
| subjects affected / exposed  | 2 / 262 (0.76%) | 5 / 307 (1.63%) | 4 / 130 (3.08%) |
| occurrences (all)            | 3               | 5               | 5               |
| Throat irritation            |                 |                 |                 |
| subjects affected / exposed  | 2 / 262 (0.76%) | 0 / 307 (0.00%) | 1 / 130 (0.77%) |
| occurrences (all)            | 2               | 0               | 1               |
| Atelectasis                  |                 |                 |                 |
| subjects affected / exposed  | 1 / 262 (0.38%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)            | 1               | 1               | 0               |
| Dry throat                   |                 |                 |                 |
| subjects affected / exposed  | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 1 / 130 (0.77%) |
| occurrences (all)            | 1               | 0               | 1               |
| Interstitial lung disease    |                 |                 |                 |

|                             |                 |                 |                 |
|-----------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed | 1 / 262 (0.38%) | 2 / 307 (0.65%) | 0 / 130 (0.00%) |
| occurrences (all)           | 2               | 4               | 0               |
| Nasal obstruction           |                 |                 |                 |
| subjects affected / exposed | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)           | 3               | 0               | 0               |
| Nasal pruritus              |                 |                 |                 |
| subjects affected / exposed | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)           | 1               | 0               | 0               |
| Nasal ulcer                 |                 |                 |                 |
| subjects affected / exposed | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)           | 1               | 0               | 0               |
| Oropharyngeal swelling      |                 |                 |                 |
| subjects affected / exposed | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)           | 1               | 0               | 0               |
| Paranasal sinus discomfort  |                 |                 |                 |
| subjects affected / exposed | 1 / 262 (0.38%) | 2 / 307 (0.65%) | 0 / 130 (0.00%) |
| occurrences (all)           | 1               | 2               | 0               |
| Pleurisy                    |                 |                 |                 |
| subjects affected / exposed | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)           | 1               | 0               | 0               |
| Pneumonitis                 |                 |                 |                 |
| subjects affected / exposed | 1 / 262 (0.38%) | 5 / 307 (1.63%) | 1 / 130 (0.77%) |
| occurrences (all)           | 1               | 5               | 1               |
| Pulmonary embolism          |                 |                 |                 |
| subjects affected / exposed | 1 / 262 (0.38%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)           | 1               | 1               | 0               |
| Pulmonary hypertension      |                 |                 |                 |
| subjects affected / exposed | 1 / 262 (0.38%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)           | 1               | 1               | 0               |
| Pulmonary mass              |                 |                 |                 |
| subjects affected / exposed | 1 / 262 (0.38%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)           | 1               | 1               | 0               |
| Rales                       |                 |                 |                 |
| subjects affected / exposed | 1 / 262 (0.38%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)           | 1               | 4               | 0               |
| Sinus congestion            |                 |                 |                 |

|                             |                 |                 |                 |
|-----------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed | 1 / 262 (0.38%) | 7 / 307 (2.28%) | 1 / 130 (0.77%) |
| occurrences (all)           | 1               | 7               | 1               |
| Sinus pain                  |                 |                 |                 |
| subjects affected / exposed | 1 / 262 (0.38%) | 3 / 307 (0.98%) | 0 / 130 (0.00%) |
| occurrences (all)           | 1               | 3               | 0               |
| Sleep apnoea syndrome       |                 |                 |                 |
| subjects affected / exposed | 1 / 262 (0.38%) | 3 / 307 (0.98%) | 0 / 130 (0.00%) |
| occurrences (all)           | 1               | 3               | 0               |
| Throat tightness            |                 |                 |                 |
| subjects affected / exposed | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)           | 1               | 0               | 0               |
| Acute respiratory failure   |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 2 / 307 (0.65%) | 1 / 130 (0.77%) |
| occurrences (all)           | 0               | 2               | 1               |
| Aspiration                  |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)           | 0               | 0               | 0               |
| Asthma                      |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)           | 0               | 1               | 0               |
| Bronchial hyperreactivity   |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)           | 0               | 1               | 0               |
| Bronchial obstruction       |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 0 / 307 (0.00%) | 1 / 130 (0.77%) |
| occurrences (all)           | 0               | 0               | 1               |
| Catarrh                     |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 2 / 307 (0.65%) | 0 / 130 (0.00%) |
| occurrences (all)           | 0               | 2               | 0               |
| Laryngeal inflammation      |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)           | 0               | 1               | 0               |
| Mediastinal shift           |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 0 / 307 (0.00%) | 1 / 130 (0.77%) |
| occurrences (all)           | 0               | 0               | 1               |
| Nasal dryness               |                 |                 |                 |

|                                |                 |                 |                 |
|--------------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed    | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)              | 0               | 1               | 0               |
| Nasal mucosal ulcer            |                 |                 |                 |
| subjects affected / exposed    | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)              | 0               | 1               | 0               |
| Nasal oedema                   |                 |                 |                 |
| subjects affected / exposed    | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)              | 0               | 1               | 0               |
| Nasal polyps                   |                 |                 |                 |
| subjects affected / exposed    | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)              | 0               | 1               | 0               |
| Nasal septum disorder          |                 |                 |                 |
| subjects affected / exposed    | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)              | 0               | 1               | 0               |
| Paranasal sinus hypersecretion |                 |                 |                 |
| subjects affected / exposed    | 0 / 262 (0.00%) | 2 / 307 (0.65%) | 0 / 130 (0.00%) |
| occurrences (all)              | 0               | 2               | 0               |
| Pharyngeal erythema            |                 |                 |                 |
| subjects affected / exposed    | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)              | 0               | 1               | 0               |
| Pharyngeal hypertrophy         |                 |                 |                 |
| subjects affected / exposed    | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)              | 0               | 1               | 0               |
| Pleuritic pain                 |                 |                 |                 |
| subjects affected / exposed    | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)              | 0               | 1               | 0               |
| Pneumothorax                   |                 |                 |                 |
| subjects affected / exposed    | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 1 / 130 (0.77%) |
| occurrences (all)              | 0               | 2               | 1               |
| Respiration abnormal           |                 |                 |                 |
| subjects affected / exposed    | 0 / 262 (0.00%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)              | 0               | 0               | 0               |
| Respiratory failure            |                 |                 |                 |
| subjects affected / exposed    | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)              | 0               | 1               | 0               |
| Respiratory tract inflammation |                 |                 |                 |

|                             |                   |                   |                   |
|-----------------------------|-------------------|-------------------|-------------------|
| subjects affected / exposed | 0 / 262 (0.00%)   | 1 / 307 (0.33%)   | 0 / 130 (0.00%)   |
| occurrences (all)           | 0                 | 1                 | 0                 |
| Rhinalgia                   |                   |                   |                   |
| subjects affected / exposed | 0 / 262 (0.00%)   | 1 / 307 (0.33%)   | 0 / 130 (0.00%)   |
| occurrences (all)           | 0                 | 1                 | 0                 |
| Rhonchi                     |                   |                   |                   |
| subjects affected / exposed | 0 / 262 (0.00%)   | 1 / 307 (0.33%)   | 0 / 130 (0.00%)   |
| occurrences (all)           | 0                 | 1                 | 0                 |
| Snoring                     |                   |                   |                   |
| subjects affected / exposed | 0 / 262 (0.00%)   | 0 / 307 (0.00%)   | 1 / 130 (0.77%)   |
| occurrences (all)           | 0                 | 0                 | 1                 |
| Sputum increased            |                   |                   |                   |
| subjects affected / exposed | 0 / 262 (0.00%)   | 0 / 307 (0.00%)   | 1 / 130 (0.77%)   |
| occurrences (all)           | 0                 | 0                 | 1                 |
| Vasomotor rhinitis          |                   |                   |                   |
| subjects affected / exposed | 0 / 262 (0.00%)   | 0 / 307 (0.00%)   | 1 / 130 (0.77%)   |
| occurrences (all)           | 0                 | 0                 | 1                 |
| Psychiatric disorders       |                   |                   |                   |
| Insomnia                    |                   |                   |                   |
| subjects affected / exposed | 28 / 262 (10.69%) | 40 / 307 (13.03%) | 19 / 130 (14.62%) |
| occurrences (all)           | 33                | 45                | 25                |
| Anxiety                     |                   |                   |                   |
| subjects affected / exposed | 14 / 262 (5.34%)  | 8 / 307 (2.61%)   | 7 / 130 (5.38%)   |
| occurrences (all)           | 15                | 9                 | 7                 |
| Agitation                   |                   |                   |                   |
| subjects affected / exposed | 6 / 262 (2.29%)   | 2 / 307 (0.65%)   | 2 / 130 (1.54%)   |
| occurrences (all)           | 6                 | 2                 | 2                 |
| Confusional state           |                   |                   |                   |
| subjects affected / exposed | 6 / 262 (2.29%)   | 16 / 307 (5.21%)  | 1 / 130 (0.77%)   |
| occurrences (all)           | 6                 | 16                | 1                 |
| Depression                  |                   |                   |                   |
| subjects affected / exposed | 5 / 262 (1.91%)   | 13 / 307 (4.23%)  | 4 / 130 (3.08%)   |
| occurrences (all)           | 5                 | 13                | 4                 |
| Restlessness                |                   |                   |                   |
| subjects affected / exposed | 2 / 262 (0.76%)   | 1 / 307 (0.33%)   | 2 / 130 (1.54%)   |
| occurrences (all)           | 2                 | 1                 | 2                 |

|                             |                 |                 |                 |
|-----------------------------|-----------------|-----------------|-----------------|
| Sleep disorder              |                 |                 |                 |
| subjects affected / exposed | 2 / 262 (0.76%) | 2 / 307 (0.65%) | 0 / 130 (0.00%) |
| occurrences (all)           | 2               | 2               | 0               |
| Delirium                    |                 |                 |                 |
| subjects affected / exposed | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)           | 1               | 0               | 0               |
| Depressed mood              |                 |                 |                 |
| subjects affected / exposed | 1 / 262 (0.38%) | 3 / 307 (0.98%) | 0 / 130 (0.00%) |
| occurrences (all)           | 1               | 4               | 0               |
| Euphoric mood               |                 |                 |                 |
| subjects affected / exposed | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)           | 2               | 0               | 0               |
| Irritability                |                 |                 |                 |
| subjects affected / exposed | 1 / 262 (0.38%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)           | 1               | 2               | 0               |
| Mood swings                 |                 |                 |                 |
| subjects affected / exposed | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)           | 1               | 0               | 0               |
| Nightmare                   |                 |                 |                 |
| subjects affected / exposed | 1 / 262 (0.38%) | 1 / 307 (0.33%) | 1 / 130 (0.77%) |
| occurrences (all)           | 1               | 1               | 1               |
| Poor quality sleep          |                 |                 |                 |
| subjects affected / exposed | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)           | 1               | 0               | 0               |
| Abnormal dreams             |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)           | 0               | 1               | 0               |
| Affect lability             |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)           | 0               | 1               | 0               |
| Bruxism                     |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)           | 0               | 2               | 0               |
| Disorientation              |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)           | 0               | 1               | 0               |

|                             |                 |                 |                 |
|-----------------------------|-----------------|-----------------|-----------------|
| Emotional disorder          |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)           | 0               | 1               | 0               |
| Hallucination               |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 2 / 307 (0.65%) | 0 / 130 (0.00%) |
| occurrences (all)           | 0               | 2               | 0               |
| Mania                       |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)           | 0               | 1               | 0               |
| Mental status changes       |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 2 / 307 (0.65%) | 1 / 130 (0.77%) |
| occurrences (all)           | 0               | 2               | 1               |
| Mood altered                |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)           | 0               | 1               | 0               |
| Nervousness                 |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 0 / 307 (0.00%) | 1 / 130 (0.77%) |
| occurrences (all)           | 0               | 0               | 1               |
| Panic attack                |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)           | 0               | 1               | 0               |
| Self-induced vomiting       |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)           | 0               | 3               | 0               |
| Product issues              |                 |                 |                 |
| Device leakage              |                 |                 |                 |
| subjects affected / exposed | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)           | 1               | 0               | 0               |
| Device breakage             |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)           | 0               | 1               | 0               |
| Device occlusion            |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 0 / 307 (0.00%) | 1 / 130 (0.77%) |
| occurrences (all)           | 0               | 0               | 2               |
| Thrombosis in device        |                 |                 |                 |

|                                                  |                      |                      |                      |
|--------------------------------------------------|----------------------|----------------------|----------------------|
| subjects affected / exposed<br>occurrences (all) | 0 / 262 (0.00%)<br>0 | 0 / 307 (0.00%)<br>0 | 0 / 130 (0.00%)<br>0 |
| Hepatobiliary disorders                          |                      |                      |                      |
| Cholecystitis acute                              |                      |                      |                      |
| subjects affected / exposed                      | 1 / 262 (0.38%)      | 0 / 307 (0.00%)      | 0 / 130 (0.00%)      |
| occurrences (all)                                | 1                    | 0                    | 0                    |
| Hepatic necrosis                                 |                      |                      |                      |
| subjects affected / exposed                      | 1 / 262 (0.38%)      | 0 / 307 (0.00%)      | 0 / 130 (0.00%)      |
| occurrences (all)                                | 1                    | 0                    | 0                    |
| Hepatitis                                        |                      |                      |                      |
| subjects affected / exposed                      | 1 / 262 (0.38%)      | 0 / 307 (0.00%)      | 0 / 130 (0.00%)      |
| occurrences (all)                                | 1                    | 0                    | 0                    |
| Hepatocellular injury                            |                      |                      |                      |
| subjects affected / exposed                      | 1 / 262 (0.38%)      | 0 / 307 (0.00%)      | 0 / 130 (0.00%)      |
| occurrences (all)                                | 3                    | 0                    | 0                    |
| Bile duct obstruction                            |                      |                      |                      |
| subjects affected / exposed                      | 0 / 262 (0.00%)      | 1 / 307 (0.33%)      | 0 / 130 (0.00%)      |
| occurrences (all)                                | 0                    | 1                    | 0                    |
| Cholecystitis                                    |                      |                      |                      |
| subjects affected / exposed                      | 0 / 262 (0.00%)      | 1 / 307 (0.33%)      | 0 / 130 (0.00%)      |
| occurrences (all)                                | 0                    | 1                    | 0                    |
| Gallbladder polyp                                |                      |                      |                      |
| subjects affected / exposed                      | 0 / 262 (0.00%)      | 1 / 307 (0.33%)      | 0 / 130 (0.00%)      |
| occurrences (all)                                | 0                    | 1                    | 0                    |
| Hepatic cirrhosis                                |                      |                      |                      |
| subjects affected / exposed                      | 0 / 262 (0.00%)      | 1 / 307 (0.33%)      | 1 / 130 (0.77%)      |
| occurrences (all)                                | 0                    | 1                    | 1                    |
| Hepatic steatosis                                |                      |                      |                      |
| subjects affected / exposed                      | 0 / 262 (0.00%)      | 1 / 307 (0.33%)      | 0 / 130 (0.00%)      |
| occurrences (all)                                | 0                    | 1                    | 0                    |
| Hepatitis acute                                  |                      |                      |                      |
| subjects affected / exposed                      | 0 / 262 (0.00%)      | 1 / 307 (0.33%)      | 0 / 130 (0.00%)      |
| occurrences (all)                                | 0                    | 2                    | 0                    |
| Hyperbilirubinaemia                              |                      |                      |                      |
| subjects affected / exposed                      | 0 / 262 (0.00%)      | 1 / 307 (0.33%)      | 0 / 130 (0.00%)      |
| occurrences (all)                                | 0                    | 2                    | 0                    |

|                                                                                           |                         |                          |                         |
|-------------------------------------------------------------------------------------------|-------------------------|--------------------------|-------------------------|
| Liver disorder<br>subjects affected / exposed<br>occurrences (all)                        | 0 / 262 (0.00%)<br>0    | 1 / 307 (0.33%)<br>1     | 0 / 130 (0.00%)<br>0    |
| Investigations                                                                            |                         |                          |                         |
| Aspartate aminotransferase increased<br>subjects affected / exposed<br>occurrences (all)  | 40 / 262 (15.27%)<br>80 | 51 / 307 (16.61%)<br>81  | 14 / 130 (10.77%)<br>23 |
| Alanine aminotransferase increased<br>subjects affected / exposed<br>occurrences (all)    | 38 / 262 (14.50%)<br>96 | 53 / 307 (17.26%)<br>107 | 13 / 130 (10.00%)<br>20 |
| Neutrophil count decreased<br>subjects affected / exposed<br>occurrences (all)            | 23 / 262 (8.78%)<br>76  | 21 / 307 (6.84%)<br>33   | 17 / 130 (13.08%)<br>31 |
| Blood creatinine increased<br>subjects affected / exposed<br>occurrences (all)            | 17 / 262 (6.49%)<br>29  | 38 / 307 (12.38%)<br>52  | 5 / 130 (3.85%)<br>6    |
| Blood lactate dehydrogenase increased<br>subjects affected / exposed<br>occurrences (all) | 14 / 262 (5.34%)<br>14  | 5 / 307 (1.63%)<br>5     | 6 / 130 (4.62%)<br>7    |
| Blood alkaline phosphatase increased<br>subjects affected / exposed<br>occurrences (all)  | 12 / 262 (4.58%)<br>14  | 14 / 307 (4.56%)<br>20   | 9 / 130 (6.92%)<br>14   |
| Weight decreased<br>subjects affected / exposed<br>occurrences (all)                      | 12 / 262 (4.58%)<br>15  | 24 / 307 (7.82%)<br>32   | 14 / 130 (10.77%)<br>19 |
| Blood bilirubin increased<br>subjects affected / exposed<br>occurrences (all)             | 9 / 262 (3.44%)<br>16   | 8 / 307 (2.61%)<br>14    | 5 / 130 (3.85%)<br>9    |
| Platelet count decreased<br>subjects affected / exposed<br>occurrences (all)              | 9 / 262 (3.44%)<br>17   | 16 / 307 (5.21%)<br>28   | 12 / 130 (9.23%)<br>27  |
| White blood cell count decreased<br>subjects affected / exposed<br>occurrences (all)      | 9 / 262 (3.44%)<br>16   | 7 / 307 (2.28%)<br>10    | 9 / 130 (6.92%)<br>25   |
| Weight increased                                                                          |                         |                          |                         |

|                                     |                 |                 |                 |
|-------------------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed         | 7 / 262 (2.67%) | 5 / 307 (1.63%) | 1 / 130 (0.77%) |
| occurrences (all)                   | 7               | 9               | 7               |
| Lymphocyte count decreased          |                 |                 |                 |
| subjects affected / exposed         | 4 / 262 (1.53%) | 6 / 307 (1.95%) | 3 / 130 (2.31%) |
| occurrences (all)                   | 9               | 8               | 5               |
| Blood magnesium decreased           |                 |                 |                 |
| subjects affected / exposed         | 3 / 262 (1.15%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)                   | 3               | 1               | 0               |
| Blood pressure increased            |                 |                 |                 |
| subjects affected / exposed         | 3 / 262 (1.15%) | 4 / 307 (1.30%) | 2 / 130 (1.54%) |
| occurrences (all)                   | 4               | 5               | 3               |
| C-reactive protein increased        |                 |                 |                 |
| subjects affected / exposed         | 3 / 262 (1.15%) | 2 / 307 (0.65%) | 0 / 130 (0.00%) |
| occurrences (all)                   | 3               | 2               | 0               |
| Hepatic enzyme increased            |                 |                 |                 |
| subjects affected / exposed         | 3 / 262 (1.15%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)                   | 5               | 0               | 0               |
| Blood uric acid increased           |                 |                 |                 |
| subjects affected / exposed         | 2 / 262 (0.76%) | 4 / 307 (1.30%) | 0 / 130 (0.00%) |
| occurrences (all)                   | 2               | 4               | 0               |
| Ejection fraction decreased         |                 |                 |                 |
| subjects affected / exposed         | 2 / 262 (0.76%) | 1 / 307 (0.33%) | 1 / 130 (0.77%) |
| occurrences (all)                   | 2               | 1               | 1               |
| Gamma-glutamyltransferase increased |                 |                 |                 |
| subjects affected / exposed         | 2 / 262 (0.76%) | 2 / 307 (0.65%) | 0 / 130 (0.00%) |
| occurrences (all)                   | 3               | 2               | 0               |
| Glomerular filtration rate          |                 |                 |                 |
| subjects affected / exposed         | 2 / 262 (0.76%) | 1 / 307 (0.33%) | 1 / 130 (0.77%) |
| occurrences (all)                   | 2               | 1               | 1               |
| Ammonia increased                   |                 |                 |                 |
| subjects affected / exposed         | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)                   | 1               | 0               | 0               |
| Blood albumin decreased             |                 |                 |                 |
| subjects affected / exposed         | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)                   | 1               | 0               | 0               |

|                                                                                       |                      |                      |                      |
|---------------------------------------------------------------------------------------|----------------------|----------------------|----------------------|
| Blood bicarbonate decreased<br>subjects affected / exposed<br>occurrences (all)       | 1 / 262 (0.38%)<br>1 | 0 / 307 (0.00%)<br>0 | 0 / 130 (0.00%)<br>0 |
| Blood calcium increased<br>subjects affected / exposed<br>occurrences (all)           | 1 / 262 (0.38%)<br>1 | 0 / 307 (0.00%)<br>0 | 0 / 130 (0.00%)<br>0 |
| Blood cholesterol increased<br>subjects affected / exposed<br>occurrences (all)       | 1 / 262 (0.38%)<br>1 | 3 / 307 (0.98%)<br>3 | 1 / 130 (0.77%)<br>1 |
| Blood glucose increased<br>subjects affected / exposed<br>occurrences (all)           | 1 / 262 (0.38%)<br>1 | 0 / 307 (0.00%)<br>0 | 0 / 130 (0.00%)<br>0 |
| Blood immunoglobulin G decreased<br>subjects affected / exposed<br>occurrences (all)  | 1 / 262 (0.38%)<br>1 | 1 / 307 (0.33%)<br>2 | 0 / 130 (0.00%)<br>0 |
| Blood urea increased<br>subjects affected / exposed<br>occurrences (all)              | 1 / 262 (0.38%)<br>1 | 2 / 307 (0.65%)<br>2 | 0 / 130 (0.00%)<br>0 |
| Blood urine present<br>subjects affected / exposed<br>occurrences (all)               | 1 / 262 (0.38%)<br>1 | 0 / 307 (0.00%)<br>0 | 0 / 130 (0.00%)<br>0 |
| Cardiac murmur<br>subjects affected / exposed<br>occurrences (all)                    | 1 / 262 (0.38%)<br>1 | 3 / 307 (0.98%)<br>3 | 1 / 130 (0.77%)<br>1 |
| Clostridium test positive<br>subjects affected / exposed<br>occurrences (all)         | 1 / 262 (0.38%)<br>1 | 0 / 307 (0.00%)<br>0 | 0 / 130 (0.00%)<br>0 |
| Coronavirus test positive<br>subjects affected / exposed<br>occurrences (all)         | 1 / 262 (0.38%)<br>1 | 0 / 307 (0.00%)<br>0 | 0 / 130 (0.00%)<br>0 |
| Cytomegalovirus test positive<br>subjects affected / exposed<br>occurrences (all)     | 1 / 262 (0.38%)<br>1 | 1 / 307 (0.33%)<br>1 | 0 / 130 (0.00%)<br>0 |
| ECG signs of myocardial ischaemia<br>subjects affected / exposed<br>occurrences (all) | 1 / 262 (0.38%)<br>1 | 0 / 307 (0.00%)<br>0 | 0 / 130 (0.00%)<br>0 |

|                                                                                                    |                      |                      |                      |
|----------------------------------------------------------------------------------------------------|----------------------|----------------------|----------------------|
| Electrocardiogram QT prolonged<br>subjects affected / exposed<br>occurrences (all)                 | 1 / 262 (0.38%)<br>1 | 2 / 307 (0.65%)<br>2 | 0 / 130 (0.00%)<br>0 |
| Haemoglobin decreased<br>subjects affected / exposed<br>occurrences (all)                          | 1 / 262 (0.38%)<br>1 | 1 / 307 (0.33%)<br>2 | 0 / 130 (0.00%)<br>0 |
| Hepatic enzyme abnormal<br>subjects affected / exposed<br>occurrences (all)                        | 1 / 262 (0.38%)<br>1 | 0 / 307 (0.00%)<br>0 | 0 / 130 (0.00%)<br>0 |
| Immunoglobulins decreased<br>subjects affected / exposed<br>occurrences (all)                      | 1 / 262 (0.38%)<br>1 | 0 / 307 (0.00%)<br>0 | 0 / 130 (0.00%)<br>0 |
| Liver function test increased<br>subjects affected / exposed<br>occurrences (all)                  | 1 / 262 (0.38%)<br>1 | 0 / 307 (0.00%)<br>0 | 0 / 130 (0.00%)<br>0 |
| Magnetic resonance imaging brain<br>abnormal<br>subjects affected / exposed<br>occurrences (all)   | 1 / 262 (0.38%)<br>1 | 0 / 307 (0.00%)<br>0 | 0 / 130 (0.00%)<br>0 |
| Prostatic specific antigen increased<br>subjects affected / exposed<br>occurrences (all)           | 1 / 262 (0.38%)<br>1 | 0 / 307 (0.00%)<br>0 | 0 / 130 (0.00%)<br>0 |
| Prothrombin time prolonged<br>subjects affected / exposed<br>occurrences (all)                     | 1 / 262 (0.38%)<br>1 | 1 / 307 (0.33%)<br>1 | 0 / 130 (0.00%)<br>0 |
| Red blood cell sedimentation rate<br>increased<br>subjects affected / exposed<br>occurrences (all) | 1 / 262 (0.38%)<br>1 | 0 / 307 (0.00%)<br>0 | 0 / 130 (0.00%)<br>0 |
| Transaminases increased<br>subjects affected / exposed<br>occurrences (all)                        | 1 / 262 (0.38%)<br>1 | 3 / 307 (0.98%)<br>4 | 1 / 130 (0.77%)<br>1 |
| Troponin increased<br>subjects affected / exposed<br>occurrences (all)                             | 1 / 262 (0.38%)<br>1 | 0 / 307 (0.00%)<br>0 | 0 / 130 (0.00%)<br>0 |
| Urinary sediment present                                                                           |                      |                      |                      |

|                                        |                 |                 |                 |
|----------------------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed            | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)                      | 1               | 0               | 0               |
| Vitamin B12 decreased                  |                 |                 |                 |
| subjects affected / exposed            | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)                      | 1               | 0               | 0               |
| Beta globulin decreased                |                 |                 |                 |
| subjects affected / exposed            | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)                      | 0               | 1               | 0               |
| Blood creatine phosphokinase increased |                 |                 |                 |
| subjects affected / exposed            | 0 / 262 (0.00%) | 0 / 307 (0.00%) | 1 / 130 (0.77%) |
| occurrences (all)                      | 0               | 0               | 2               |
| Blood immunoglobulin A decreased       |                 |                 |                 |
| subjects affected / exposed            | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)                      | 0               | 1               | 0               |
| Blood immunoglobulin M increased       |                 |                 |                 |
| subjects affected / exposed            | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)                      | 0               | 1               | 0               |
| Blood iron decreased                   |                 |                 |                 |
| subjects affected / exposed            | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)                      | 0               | 1               | 0               |
| Blood potassium decreased              |                 |                 |                 |
| subjects affected / exposed            | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)                      | 0               | 1               | 0               |
| Blood prolactin increased              |                 |                 |                 |
| subjects affected / exposed            | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)                      | 0               | 1               | 0               |
| Blood testosterone decreased           |                 |                 |                 |
| subjects affected / exposed            | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)                      | 0               | 1               | 0               |
| Blood viscosity increased              |                 |                 |                 |
| subjects affected / exposed            | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)                      | 0               | 1               | 0               |
| Body temperature decreased             |                 |                 |                 |
| subjects affected / exposed            | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)                      | 0               | 4               | 0               |

|                                                                                                                       |                      |                      |                      |
|-----------------------------------------------------------------------------------------------------------------------|----------------------|----------------------|----------------------|
| Body temperature increased<br>subjects affected / exposed<br>occurrences (all)                                        | 0 / 262 (0.00%)<br>0 | 1 / 307 (0.33%)<br>1 | 1 / 130 (0.77%)<br>1 |
| Bone density decreased<br>subjects affected / exposed<br>occurrences (all)                                            | 0 / 262 (0.00%)<br>0 | 1 / 307 (0.33%)<br>1 | 0 / 130 (0.00%)<br>0 |
| Breath sounds abnormal<br>subjects affected / exposed<br>occurrences (all)                                            | 0 / 262 (0.00%)<br>0 | 1 / 307 (0.33%)<br>1 | 0 / 130 (0.00%)<br>0 |
| Eastern Cooperative Oncology Group<br>performance status worsened<br>subjects affected / exposed<br>occurrences (all) | 0 / 262 (0.00%)<br>0 | 1 / 307 (0.33%)<br>1 | 0 / 130 (0.00%)<br>0 |
| Faecal calprotectin increased<br>subjects affected / exposed<br>occurrences (all)                                     | 0 / 262 (0.00%)<br>0 | 1 / 307 (0.33%)<br>1 | 0 / 130 (0.00%)<br>0 |
| Haemoglobin increased<br>subjects affected / exposed<br>occurrences (all)                                             | 0 / 262 (0.00%)<br>0 | 1 / 307 (0.33%)<br>1 | 0 / 130 (0.00%)<br>0 |
| Haemophilus test positive<br>subjects affected / exposed<br>occurrences (all)                                         | 0 / 262 (0.00%)<br>0 | 1 / 307 (0.33%)<br>1 | 0 / 130 (0.00%)<br>0 |
| Heart rate increased<br>subjects affected / exposed<br>occurrences (all)                                              | 0 / 262 (0.00%)<br>0 | 0 / 307 (0.00%)<br>0 | 1 / 130 (0.77%)<br>1 |
| Human rhinovirus positive<br>subjects affected / exposed<br>occurrences (all)                                         | 0 / 262 (0.00%)<br>0 | 0 / 307 (0.00%)<br>0 | 1 / 130 (0.77%)<br>1 |
| Immature granulocyte count<br>increased<br>subjects affected / exposed<br>occurrences (all)                           | 0 / 262 (0.00%)<br>0 | 1 / 307 (0.33%)<br>1 | 0 / 130 (0.00%)<br>0 |
| Immunoglobulins increased<br>subjects affected / exposed<br>occurrences (all)                                         | 0 / 262 (0.00%)<br>0 | 1 / 307 (0.33%)<br>1 | 0 / 130 (0.00%)<br>0 |
| International normalised ratio<br>increased                                                                           |                      |                      |                      |

|                                   |                 |                 |                 |
|-----------------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed       | 0 / 262 (0.00%) | 4 / 307 (1.30%) | 0 / 130 (0.00%) |
| occurrences (all)                 | 0               | 7               | 0               |
| Light chain analysis decreased    |                 |                 |                 |
| subjects affected / exposed       | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)                 | 0               | 1               | 0               |
| Light chain analysis increased    |                 |                 |                 |
| subjects affected / exposed       | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)                 | 0               | 1               | 0               |
| Lipase increased                  |                 |                 |                 |
| subjects affected / exposed       | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 1 / 130 (0.77%) |
| occurrences (all)                 | 0               | 2               | 3               |
| Low density lipoprotein increased |                 |                 |                 |
| subjects affected / exposed       | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)                 | 0               | 1               | 0               |
| Lymphocyte count abnormal         |                 |                 |                 |
| subjects affected / exposed       | 0 / 262 (0.00%) | 0 / 307 (0.00%) | 1 / 130 (0.77%) |
| occurrences (all)                 | 0               | 0               | 1               |
| Lymphocyte count increased        |                 |                 |                 |
| subjects affected / exposed       | 0 / 262 (0.00%) | 2 / 307 (0.65%) | 0 / 130 (0.00%) |
| occurrences (all)                 | 0               | 3               | 0               |
| Monocyte count decreased          |                 |                 |                 |
| subjects affected / exposed       | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)                 | 0               | 1               | 0               |
| Neutrophil count increased        |                 |                 |                 |
| subjects affected / exposed       | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)                 | 0               | 1               | 0               |
| Pedal pulse decreased             |                 |                 |                 |
| subjects affected / exposed       | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)                 | 0               | 1               | 0               |
| Platelet count increased          |                 |                 |                 |
| subjects affected / exposed       | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)                 | 0               | 1               | 0               |
| Protein total decreased           |                 |                 |                 |
| subjects affected / exposed       | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)                 | 0               | 1               | 0               |
| Protein urine present             |                 |                 |                 |

|                                                |                   |                  |                  |
|------------------------------------------------|-------------------|------------------|------------------|
| subjects affected / exposed                    | 0 / 262 (0.00%)   | 1 / 307 (0.33%)  | 0 / 130 (0.00%)  |
| occurrences (all)                              | 0                 | 1                | 0                |
| Red cell distribution width increased          |                   |                  |                  |
| subjects affected / exposed                    | 0 / 262 (0.00%)   | 1 / 307 (0.33%)  | 0 / 130 (0.00%)  |
| occurrences (all)                              | 0                 | 1                | 0                |
| SARS-CoV-2 test positive                       |                   |                  |                  |
| subjects affected / exposed                    | 0 / 262 (0.00%)   | 2 / 307 (0.65%)  | 0 / 130 (0.00%)  |
| occurrences (all)                              | 0                 | 2                | 0                |
| Serum ferritin decreased                       |                   |                  |                  |
| subjects affected / exposed                    | 0 / 262 (0.00%)   | 2 / 307 (0.65%)  | 0 / 130 (0.00%)  |
| occurrences (all)                              | 0                 | 2                | 0                |
| Troponin I increased                           |                   |                  |                  |
| subjects affected / exposed                    | 0 / 262 (0.00%)   | 0 / 307 (0.00%)  | 1 / 130 (0.77%)  |
| occurrences (all)                              | 0                 | 0                | 1                |
| Vitamin D decreased                            |                   |                  |                  |
| subjects affected / exposed                    | 0 / 262 (0.00%)   | 0 / 307 (0.00%)  | 2 / 130 (1.54%)  |
| occurrences (all)                              | 0                 | 0                | 2                |
| White blood cell count increased               |                   |                  |                  |
| subjects affected / exposed                    | 0 / 262 (0.00%)   | 1 / 307 (0.33%)  | 0 / 130 (0.00%)  |
| occurrences (all)                              | 0                 | 1                | 0                |
| Injury, poisoning and procedural complications |                   |                  |                  |
| Infusion related reaction                      |                   |                  |                  |
| subjects affected / exposed                    | 30 / 262 (11.45%) | 2 / 307 (0.65%)  | 4 / 130 (3.08%)  |
| occurrences (all)                              | 35                | 2                | 5                |
| Fall                                           |                   |                  |                  |
| subjects affected / exposed                    | 15 / 262 (5.73%)  | 17 / 307 (5.54%) | 11 / 130 (8.46%) |
| occurrences (all)                              | 16                | 19               | 12               |
| Skin laceration                                |                   |                  |                  |
| subjects affected / exposed                    | 3 / 262 (1.15%)   | 0 / 307 (0.00%)  | 2 / 130 (1.54%)  |
| occurrences (all)                              | 3                 | 0                | 2                |
| Limb injury                                    |                   |                  |                  |
| subjects affected / exposed                    | 2 / 262 (0.76%)   | 0 / 307 (0.00%)  | 0 / 130 (0.00%)  |
| occurrences (all)                              | 2                 | 0                | 0                |
| Procedural pain                                |                   |                  |                  |

|                                  |                 |                 |                 |
|----------------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed      | 2 / 262 (0.76%) | 2 / 307 (0.65%) | 0 / 130 (0.00%) |
| occurrences (all)                | 2               | 2               | 0               |
| Accidental overdose              |                 |                 |                 |
| subjects affected / exposed      | 1 / 262 (0.38%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)                | 1               | 1               | 0               |
| Arthropod bite                   |                 |                 |                 |
| subjects affected / exposed      | 1 / 262 (0.38%) | 3 / 307 (0.98%) | 0 / 130 (0.00%) |
| occurrences (all)                | 1               | 3               | 0               |
| Arthropod sting                  |                 |                 |                 |
| subjects affected / exposed      | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)                | 1               | 0               | 0               |
| Lumbar vertebral fracture        |                 |                 |                 |
| subjects affected / exposed      | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)                | 2               | 0               | 0               |
| Radius fracture                  |                 |                 |                 |
| subjects affected / exposed      | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)                | 1               | 0               | 0               |
| Rib fracture                     |                 |                 |                 |
| subjects affected / exposed      | 1 / 262 (0.38%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)                | 1               | 1               | 0               |
| Skin abrasion                    |                 |                 |                 |
| subjects affected / exposed      | 1 / 262 (0.38%) | 2 / 307 (0.65%) | 2 / 130 (1.54%) |
| occurrences (all)                | 1               | 2               | 2               |
| Thoracic vertebral fracture      |                 |                 |                 |
| subjects affected / exposed      | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)                | 1               | 0               | 0               |
| Traumatic intracranial haematoma |                 |                 |                 |
| subjects affected / exposed      | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)                | 1               | 0               | 0               |
| Wound secretion                  |                 |                 |                 |
| subjects affected / exposed      | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)                | 1               | 0               | 0               |
| Ankle fracture                   |                 |                 |                 |
| subjects affected / exposed      | 0 / 262 (0.00%) | 0 / 307 (0.00%) | 1 / 130 (0.77%) |
| occurrences (all)                | 0               | 0               | 1               |
| Compression fracture             |                 |                 |                 |

|                             |                 |                 |                 |
|-----------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 262 (0.00%) | 2 / 307 (0.65%) | 0 / 130 (0.00%) |
| occurrences (all)           | 0               | 2               | 0               |
| Concussion                  |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)           | 0               | 0               | 0               |
| Foreign body in ear         |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)           | 0               | 1               | 0               |
| Hand fracture               |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)           | 0               | 1               | 0               |
| Head injury                 |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 0 / 307 (0.00%) | 1 / 130 (0.77%) |
| occurrences (all)           | 0               | 0               | 1               |
| Hip fracture                |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 0 / 307 (0.00%) | 2 / 130 (1.54%) |
| occurrences (all)           | 0               | 0               | 2               |
| Joint injury                |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)           | 0               | 1               | 0               |
| Lip injury                  |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 0 / 307 (0.00%) | 1 / 130 (0.77%) |
| occurrences (all)           | 0               | 0               | 1               |
| Meniscus injury             |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 1 / 130 (0.77%) |
| occurrences (all)           | 0               | 1               | 1               |
| Muscle strain               |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 1 / 130 (0.77%) |
| occurrences (all)           | 0               | 1               | 1               |
| Overdose                    |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)           | 0               | 1               | 0               |
| Periorbital haematoma       |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 0 / 307 (0.00%) | 1 / 130 (0.77%) |
| occurrences (all)           | 0               | 0               | 1               |
| Procedural hypotension      |                 |                 |                 |

|                                  |                 |                 |                 |
|----------------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed      | 0 / 262 (0.00%) | 0 / 307 (0.00%) | 1 / 130 (0.77%) |
| occurrences (all)                | 0               | 0               | 1               |
| Product administration error     |                 |                 |                 |
| subjects affected / exposed      | 0 / 262 (0.00%) | 0 / 307 (0.00%) | 1 / 130 (0.77%) |
| occurrences (all)                | 0               | 0               | 1               |
| Skin injury                      |                 |                 |                 |
| subjects affected / exposed      | 0 / 262 (0.00%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)                | 0               | 0               | 0               |
| Spinal compression fracture      |                 |                 |                 |
| subjects affected / exposed      | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 1 / 130 (0.77%) |
| occurrences (all)                | 0               | 1               | 1               |
| Spinal fracture                  |                 |                 |                 |
| subjects affected / exposed      | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)                | 0               | 1               | 0               |
| Splenic injury                   |                 |                 |                 |
| subjects affected / exposed      | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)                | 0               | 1               | 0               |
| Stress fracture                  |                 |                 |                 |
| subjects affected / exposed      | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)                | 0               | 1               | 0               |
| Subdural haematoma               |                 |                 |                 |
| subjects affected / exposed      | 0 / 262 (0.00%) | 0 / 307 (0.00%) | 1 / 130 (0.77%) |
| occurrences (all)                | 0               | 0               | 1               |
| Tendon rupture                   |                 |                 |                 |
| subjects affected / exposed      | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)                | 0               | 1               | 0               |
| Thermal burn                     |                 |                 |                 |
| subjects affected / exposed      | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)                | 0               | 1               | 0               |
| Tibia fracture                   |                 |                 |                 |
| subjects affected / exposed      | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)                | 0               | 1               | 0               |
| Wound complication               |                 |                 |                 |
| subjects affected / exposed      | 0 / 262 (0.00%) | 0 / 307 (0.00%) | 1 / 130 (0.77%) |
| occurrences (all)                | 0               | 0               | 1               |
| Congenital, familial and genetic |                 |                 |                 |

|                                      |                 |                 |                 |
|--------------------------------------|-----------------|-----------------|-----------------|
| disorders                            |                 |                 |                 |
| Phimosis                             |                 |                 |                 |
| subjects affected / exposed          | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)                    | 0               | 1               | 0               |
| Cardiac disorders                    |                 |                 |                 |
| Tachycardia                          |                 |                 |                 |
| subjects affected / exposed          | 9 / 262 (3.44%) | 8 / 307 (2.61%) | 7 / 130 (5.38%) |
| occurrences (all)                    | 10              | 8               | 7               |
| Atrial fibrillation                  |                 |                 |                 |
| subjects affected / exposed          | 4 / 262 (1.53%) | 5 / 307 (1.63%) | 5 / 130 (3.85%) |
| occurrences (all)                    | 7               | 6               | 5               |
| Palpitations                         |                 |                 |                 |
| subjects affected / exposed          | 4 / 262 (1.53%) | 4 / 307 (1.30%) | 5 / 130 (3.85%) |
| occurrences (all)                    | 9               | 4               | 5               |
| Angina pectoris                      |                 |                 |                 |
| subjects affected / exposed          | 3 / 262 (1.15%) | 2 / 307 (0.65%) | 0 / 130 (0.00%) |
| occurrences (all)                    | 3               | 3               | 0               |
| Cardiac failure                      |                 |                 |                 |
| subjects affected / exposed          | 2 / 262 (0.76%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)                    | 2               | 0               | 0               |
| Pericardial effusion                 |                 |                 |                 |
| subjects affected / exposed          | 2 / 262 (0.76%) | 3 / 307 (0.98%) | 1 / 130 (0.77%) |
| occurrences (all)                    | 2               | 3               | 1               |
| Sinus tachycardia                    |                 |                 |                 |
| subjects affected / exposed          | 2 / 262 (0.76%) | 5 / 307 (1.63%) | 2 / 130 (1.54%) |
| occurrences (all)                    | 2               | 6               | 2               |
| Atrial tachycardia                   |                 |                 |                 |
| subjects affected / exposed          | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)                    | 1               | 0               | 0               |
| Atrioventricular block complete      |                 |                 |                 |
| subjects affected / exposed          | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)                    | 1               | 0               | 0               |
| Atrioventricular block second degree |                 |                 |                 |
| subjects affected / exposed          | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)                    | 1               | 0               | 0               |
| Cardiac failure congestive           |                 |                 |                 |

|                              |                 |                 |                 |
|------------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed  | 1 / 262 (0.38%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)            | 1               | 1               | 0               |
| Cardiomyopathy               |                 |                 |                 |
| subjects affected / exposed  | 1 / 262 (0.38%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)            | 1               | 1               | 0               |
| Coronary artery disease      |                 |                 |                 |
| subjects affected / exposed  | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)            | 1               | 0               | 0               |
| Sinus bradycardia            |                 |                 |                 |
| subjects affected / exposed  | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)            | 1               | 0               | 0               |
| Ventricular extrasystoles    |                 |                 |                 |
| subjects affected / exposed  | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)            | 1               | 0               | 0               |
| Aortic valve incompetence    |                 |                 |                 |
| subjects affected / exposed  | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)            | 0               | 1               | 0               |
| Arrhythmia                   |                 |                 |                 |
| subjects affected / exposed  | 0 / 262 (0.00%) | 0 / 307 (0.00%) | 2 / 130 (1.54%) |
| occurrences (all)            | 0               | 0               | 2               |
| Bradycardia                  |                 |                 |                 |
| subjects affected / exposed  | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)            | 0               | 1               | 0               |
| Cardiovascular insufficiency |                 |                 |                 |
| subjects affected / exposed  | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)            | 0               | 2               | 0               |
| Extrasystoles                |                 |                 |                 |
| subjects affected / exposed  | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)            | 0               | 1               | 0               |
| Mitral valve incompetence    |                 |                 |                 |
| subjects affected / exposed  | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)            | 0               | 1               | 0               |
| Pericarditis constrictive    |                 |                 |                 |
| subjects affected / exposed  | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)            | 0               | 1               | 0               |
| Supraventricular tachycardia |                 |                 |                 |

|                                                  |                      |                      |                      |
|--------------------------------------------------|----------------------|----------------------|----------------------|
| subjects affected / exposed<br>occurrences (all) | 0 / 262 (0.00%)<br>0 | 1 / 307 (0.33%)<br>1 | 1 / 130 (0.77%)<br>1 |
| Nervous system disorders                         |                      |                      |                      |
| Headache                                         |                      |                      |                      |
| subjects affected / exposed                      | 49 / 262 (18.70%)    | 50 / 307 (16.29%)    | 15 / 130 (11.54%)    |
| occurrences (all)                                | 67                   | 81                   | 18                   |
| Dizziness                                        |                      |                      |                      |
| subjects affected / exposed                      | 44 / 262 (16.79%)    | 51 / 307 (16.61%)    | 16 / 130 (12.31%)    |
| occurrences (all)                                | 50                   | 63                   | 21                   |
| Dysgeusia                                        |                      |                      |                      |
| subjects affected / exposed                      | 19 / 262 (7.25%)     | 27 / 307 (8.79%)     | 8 / 130 (6.15%)      |
| occurrences (all)                                | 19                   | 29                   | 10                   |
| Paraesthesia                                     |                      |                      |                      |
| subjects affected / exposed                      | 14 / 262 (5.34%)     | 10 / 307 (3.26%)     | 0 / 130 (0.00%)      |
| occurrences (all)                                | 20                   | 15                   | 0                    |
| Tremor                                           |                      |                      |                      |
| subjects affected / exposed                      | 13 / 262 (4.96%)     | 14 / 307 (4.56%)     | 9 / 130 (6.92%)      |
| occurrences (all)                                | 15                   | 16                   | 16                   |
| Neuropathy peripheral                            |                      |                      |                      |
| subjects affected / exposed                      | 7 / 262 (2.67%)      | 7 / 307 (2.28%)      | 3 / 130 (2.31%)      |
| occurrences (all)                                | 7                    | 7                    | 3                    |
| Somnolence                                       |                      |                      |                      |
| subjects affected / exposed                      | 6 / 262 (2.29%)      | 8 / 307 (2.61%)      | 1 / 130 (0.77%)      |
| occurrences (all)                                | 6                    | 10                   | 1                    |
| Memory impairment                                |                      |                      |                      |
| subjects affected / exposed                      | 5 / 262 (1.91%)      | 7 / 307 (2.28%)      | 2 / 130 (1.54%)      |
| occurrences (all)                                | 5                    | 8                    | 2                    |
| Peripheral sensory neuropathy                    |                      |                      |                      |
| subjects affected / exposed                      | 5 / 262 (1.91%)      | 6 / 307 (1.95%)      | 6 / 130 (4.62%)      |
| occurrences (all)                                | 5                    | 6                    | 8                    |
| Syncope                                          |                      |                      |                      |
| subjects affected / exposed                      | 3 / 262 (1.15%)      | 5 / 307 (1.63%)      | 3 / 130 (2.31%)      |
| occurrences (all)                                | 3                    | 5                    | 4                    |
| Dysarthria                                       |                      |                      |                      |
| subjects affected / exposed                      | 2 / 262 (0.76%)      | 0 / 307 (0.00%)      | 0 / 130 (0.00%)      |
| occurrences (all)                                | 2                    | 0                    | 0                    |

|                             |                 |                 |                 |
|-----------------------------|-----------------|-----------------|-----------------|
| Dyskinesia                  |                 |                 |                 |
| subjects affected / exposed | 2 / 262 (0.76%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)           | 2               | 1               | 0               |
| Hypoaesthesia               |                 |                 |                 |
| subjects affected / exposed | 2 / 262 (0.76%) | 3 / 307 (0.98%) | 1 / 130 (0.77%) |
| occurrences (all)           | 2               | 3               | 1               |
| Lethargy                    |                 |                 |                 |
| subjects affected / exposed | 2 / 262 (0.76%) | 2 / 307 (0.65%) | 2 / 130 (1.54%) |
| occurrences (all)           | 2               | 2               | 2               |
| Taste disorder              |                 |                 |                 |
| subjects affected / exposed | 2 / 262 (0.76%) | 7 / 307 (2.28%) | 2 / 130 (1.54%) |
| occurrences (all)           | 2               | 7               | 2               |
| Amnesia                     |                 |                 |                 |
| subjects affected / exposed | 1 / 262 (0.38%) | 5 / 307 (1.63%) | 1 / 130 (0.77%) |
| occurrences (all)           | 1               | 6               | 1               |
| Aphasia                     |                 |                 |                 |
| subjects affected / exposed | 1 / 262 (0.38%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)           | 1               | 1               | 0               |
| Balance disorder            |                 |                 |                 |
| subjects affected / exposed | 1 / 262 (0.38%) | 2 / 307 (0.65%) | 2 / 130 (1.54%) |
| occurrences (all)           | 1               | 2               | 3               |
| Burning feet syndrome       |                 |                 |                 |
| subjects affected / exposed | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)           | 1               | 0               | 0               |
| Carotid artery dissection   |                 |                 |                 |
| subjects affected / exposed | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)           | 1               | 0               | 0               |
| Disturbance in attention    |                 |                 |                 |
| subjects affected / exposed | 1 / 262 (0.38%) | 2 / 307 (0.65%) | 0 / 130 (0.00%) |
| occurrences (all)           | 1               | 2               | 0               |
| Dizziness postural          |                 |                 |                 |
| subjects affected / exposed | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)           | 1               | 0               | 0               |
| Extrapyramidal disorder     |                 |                 |                 |
| subjects affected / exposed | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)           | 1               | 0               | 0               |

|                                 |                 |                 |                 |
|---------------------------------|-----------------|-----------------|-----------------|
| Facial paralysis                |                 |                 |                 |
| subjects affected / exposed     | 1 / 262 (0.38%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)               | 1               | 1               | 0               |
| Loss of consciousness           |                 |                 |                 |
| subjects affected / exposed     | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)               | 1               | 0               | 0               |
| Muscle contractions involuntary |                 |                 |                 |
| subjects affected / exposed     | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)               | 1               | 0               | 0               |
| Neuralgia                       |                 |                 |                 |
| subjects affected / exposed     | 1 / 262 (0.38%) | 2 / 307 (0.65%) | 1 / 130 (0.77%) |
| occurrences (all)               | 1               | 5               | 1               |
| Notalgia paraesthetica          |                 |                 |                 |
| subjects affected / exposed     | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)               | 1               | 0               | 0               |
| Presyncope                      |                 |                 |                 |
| subjects affected / exposed     | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 1 / 130 (0.77%) |
| occurrences (all)               | 1               | 0               | 1               |
| Restless legs syndrome          |                 |                 |                 |
| subjects affected / exposed     | 1 / 262 (0.38%) | 2 / 307 (0.65%) | 0 / 130 (0.00%) |
| occurrences (all)               | 1               | 2               | 0               |
| Seizure                         |                 |                 |                 |
| subjects affected / exposed     | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)               | 1               | 0               | 0               |
| Ageusia                         |                 |                 |                 |
| subjects affected / exposed     | 0 / 262 (0.00%) | 2 / 307 (0.65%) | 0 / 130 (0.00%) |
| occurrences (all)               | 0               | 2               | 0               |
| Anosmia                         |                 |                 |                 |
| subjects affected / exposed     | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)               | 0               | 1               | 0               |
| Burning sensation               |                 |                 |                 |
| subjects affected / exposed     | 0 / 262 (0.00%) | 2 / 307 (0.65%) | 0 / 130 (0.00%) |
| occurrences (all)               | 0               | 2               | 0               |
| Carpal tunnel syndrome          |                 |                 |                 |
| subjects affected / exposed     | 0 / 262 (0.00%) | 2 / 307 (0.65%) | 0 / 130 (0.00%) |
| occurrences (all)               | 0               | 2               | 0               |

|                                  |                 |                 |                 |
|----------------------------------|-----------------|-----------------|-----------------|
| Cervical radiculopathy           |                 |                 |                 |
| subjects affected / exposed      | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 1 / 130 (0.77%) |
| occurrences (all)                | 0               | 2               | 1               |
| Cognitive disorder               |                 |                 |                 |
| subjects affected / exposed      | 0 / 262 (0.00%) | 2 / 307 (0.65%) | 1 / 130 (0.77%) |
| occurrences (all)                | 0               | 2               | 1               |
| Coordination abnormal            |                 |                 |                 |
| subjects affected / exposed      | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)                | 0               | 1               | 0               |
| Depressed level of consciousness |                 |                 |                 |
| subjects affected / exposed      | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 1 / 130 (0.77%) |
| occurrences (all)                | 0               | 1               | 1               |
| Encephalopathy                   |                 |                 |                 |
| subjects affected / exposed      | 0 / 262 (0.00%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)                | 0               | 0               | 0               |
| Haemorrhage intracranial         |                 |                 |                 |
| subjects affected / exposed      | 0 / 262 (0.00%) | 0 / 307 (0.00%) | 1 / 130 (0.77%) |
| occurrences (all)                | 0               | 0               | 1               |
| Head discomfort                  |                 |                 |                 |
| subjects affected / exposed      | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)                | 0               | 1               | 0               |
| Hemiparesis                      |                 |                 |                 |
| subjects affected / exposed      | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 1 / 130 (0.77%) |
| occurrences (all)                | 0               | 1               | 1               |
| Hypogeusia                       |                 |                 |                 |
| subjects affected / exposed      | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)                | 0               | 1               | 0               |
| Intracranial aneurysm            |                 |                 |                 |
| subjects affected / exposed      | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)                | 0               | 1               | 0               |
| Lumbar radiculopathy             |                 |                 |                 |
| subjects affected / exposed      | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)                | 0               | 1               | 0               |
| Metabolic encephalopathy         |                 |                 |                 |
| subjects affected / exposed      | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)                | 0               | 1               | 0               |

|                             |                 |                 |                 |
|-----------------------------|-----------------|-----------------|-----------------|
| Nerve compression           |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 1 / 130 (0.77%) |
| occurrences (all)           | 0               | 1               | 1               |
| Parosmia                    |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 0 / 307 (0.00%) | 1 / 130 (0.77%) |
| occurrences (all)           | 0               | 0               | 1               |
| Peripheral motor neuropathy |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)           | 0               | 1               | 0               |
| Polyneuropathy              |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 2 / 307 (0.65%) | 0 / 130 (0.00%) |
| occurrences (all)           | 0               | 2               | 0               |
| Post herpetic neuralgia     |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 0 / 307 (0.00%) | 2 / 130 (1.54%) |
| occurrences (all)           | 0               | 0               | 2               |
| Psychomotor hyperactivity   |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)           | 0               | 1               | 0               |
| Sciatica                    |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 3 / 307 (0.98%) | 0 / 130 (0.00%) |
| occurrences (all)           | 0               | 4               | 0               |
| Sensory loss                |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 0 / 307 (0.00%) | 1 / 130 (0.77%) |
| occurrences (all)           | 0               | 0               | 1               |
| Sinus headache              |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 0 / 307 (0.00%) | 1 / 130 (0.77%) |
| occurrences (all)           | 0               | 0               | 1               |
| Spinal cord compression     |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)           | 0               | 1               | 0               |
| Trigeminal neuralgia        |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)           | 0               | 1               | 0               |
| Vascular headache           |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)           | 0               | 1               | 0               |

|                                      |                   |                   |                   |
|--------------------------------------|-------------------|-------------------|-------------------|
| Blood and lymphatic system disorders |                   |                   |                   |
| Neutropenia                          |                   |                   |                   |
| subjects affected / exposed          | 48 / 262 (18.32%) | 28 / 307 (9.12%)  | 42 / 130 (32.31%) |
| occurrences (all)                    | 88                | 70                | 113               |
| Anaemia                              |                   |                   |                   |
| subjects affected / exposed          | 33 / 262 (12.60%) | 33 / 307 (10.75%) | 30 / 130 (23.08%) |
| occurrences (all)                    | 46                | 59                | 71                |
| Thrombocytopenia                     |                   |                   |                   |
| subjects affected / exposed          | 9 / 262 (3.44%)   | 16 / 307 (5.21%)  | 17 / 130 (13.08%) |
| occurrences (all)                    | 24                | 39                | 39                |
| Lymph node pain                      |                   |                   |                   |
| subjects affected / exposed          | 6 / 262 (2.29%)   | 1 / 307 (0.33%)   | 0 / 130 (0.00%)   |
| occurrences (all)                    | 6                 | 1                 | 0                 |
| Lymphopenia                          |                   |                   |                   |
| subjects affected / exposed          | 4 / 262 (1.53%)   | 0 / 307 (0.00%)   | 2 / 130 (1.54%)   |
| occurrences (all)                    | 5                 | 0                 | 3                 |
| Leukopenia                           |                   |                   |                   |
| subjects affected / exposed          | 3 / 262 (1.15%)   | 6 / 307 (1.95%)   | 9 / 130 (6.92%)   |
| occurrences (all)                    | 4                 | 10                | 24                |
| Febrile neutropenia                  |                   |                   |                   |
| subjects affected / exposed          | 2 / 262 (0.76%)   | 1 / 307 (0.33%)   | 2 / 130 (1.54%)   |
| occurrences (all)                    | 2                 | 1                 | 2                 |
| Lymphadenopathy                      |                   |                   |                   |
| subjects affected / exposed          | 2 / 262 (0.76%)   | 1 / 307 (0.33%)   | 4 / 130 (3.08%)   |
| occurrences (all)                    | 2                 | 1                 | 4                 |
| Haemorrhagic diathesis               |                   |                   |                   |
| subjects affected / exposed          | 1 / 262 (0.38%)   | 0 / 307 (0.00%)   | 0 / 130 (0.00%)   |
| occurrences (all)                    | 1                 | 0                 | 0                 |
| Normochromic anaemia                 |                   |                   |                   |
| subjects affected / exposed          | 1 / 262 (0.38%)   | 0 / 307 (0.00%)   | 0 / 130 (0.00%)   |
| occurrences (all)                    | 1                 | 0                 | 0                 |
| Blood loss anaemia                   |                   |                   |                   |
| subjects affected / exposed          | 0 / 262 (0.00%)   | 0 / 307 (0.00%)   | 2 / 130 (1.54%)   |
| occurrences (all)                    | 0                 | 0                 | 2                 |
| Bone marrow failure                  |                   |                   |                   |

|                              |                 |                 |                 |
|------------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed  | 0 / 262 (0.00%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)            | 0               | 0               | 0               |
| Eosinophilia                 |                 |                 |                 |
| subjects affected / exposed  | 0 / 262 (0.00%) | 2 / 307 (0.65%) | 0 / 130 (0.00%) |
| occurrences (all)            | 0               | 2               | 0               |
| Iron deficiency anaemia      |                 |                 |                 |
| subjects affected / exposed  | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 2 / 130 (1.54%) |
| occurrences (all)            | 0               | 1               | 2               |
| Leukocytosis                 |                 |                 |                 |
| subjects affected / exposed  | 0 / 262 (0.00%) | 3 / 307 (0.98%) | 1 / 130 (0.77%) |
| occurrences (all)            | 0               | 3               | 1               |
| Lymphocytosis                |                 |                 |                 |
| subjects affected / exposed  | 0 / 262 (0.00%) | 4 / 307 (1.30%) | 0 / 130 (0.00%) |
| occurrences (all)            | 0               | 8               | 0               |
| Macrocytosis                 |                 |                 |                 |
| subjects affected / exposed  | 0 / 262 (0.00%) | 0 / 307 (0.00%) | 1 / 130 (0.77%) |
| occurrences (all)            | 0               | 0               | 1               |
| Microcytic anaemia           |                 |                 |                 |
| subjects affected / exposed  | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)            | 0               | 1               | 0               |
| Pancytopenia                 |                 |                 |                 |
| subjects affected / exposed  | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)            | 0               | 1               | 0               |
| Paratracheal lymphadenopathy |                 |                 |                 |
| subjects affected / exposed  | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)            | 0               | 1               | 0               |
| Splenic infarction           |                 |                 |                 |
| subjects affected / exposed  | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)            | 0               | 1               | 0               |
| Ear and labyrinth disorders  |                 |                 |                 |
| Tinnitus                     |                 |                 |                 |
| subjects affected / exposed  | 7 / 262 (2.67%) | 9 / 307 (2.93%) | 2 / 130 (1.54%) |
| occurrences (all)            | 7               | 10              | 2               |
| Ear pain                     |                 |                 |                 |
| subjects affected / exposed  | 6 / 262 (2.29%) | 5 / 307 (1.63%) | 1 / 130 (0.77%) |
| occurrences (all)            | 7               | 5               | 1               |

|                             |                 |                 |                 |
|-----------------------------|-----------------|-----------------|-----------------|
| Vertigo                     |                 |                 |                 |
| subjects affected / exposed | 2 / 262 (0.76%) | 1 / 307 (0.33%) | 1 / 130 (0.77%) |
| occurrences (all)           | 3               | 1               | 1               |
| Deafness                    |                 |                 |                 |
| subjects affected / exposed | 1 / 262 (0.38%) | 3 / 307 (0.98%) | 0 / 130 (0.00%) |
| occurrences (all)           | 1               | 3               | 0               |
| Ear congestion              |                 |                 |                 |
| subjects affected / exposed | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 1 / 130 (0.77%) |
| occurrences (all)           | 1               | 0               | 1               |
| Ear pruritus                |                 |                 |                 |
| subjects affected / exposed | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)           | 1               | 0               | 0               |
| Ear swelling                |                 |                 |                 |
| subjects affected / exposed | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)           | 1               | 0               | 0               |
| External ear inflammation   |                 |                 |                 |
| subjects affected / exposed | 1 / 262 (0.38%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)           | 1               | 1               | 0               |
| Hypoacusis                  |                 |                 |                 |
| subjects affected / exposed | 1 / 262 (0.38%) | 3 / 307 (0.98%) | 1 / 130 (0.77%) |
| occurrences (all)           | 1               | 3               | 1               |
| Otorrhoea                   |                 |                 |                 |
| subjects affected / exposed | 1 / 262 (0.38%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)           | 1               | 1               | 0               |
| Vertigo positional          |                 |                 |                 |
| subjects affected / exposed | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)           | 1               | 0               | 0               |
| Deafness unilateral         |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 1 / 130 (0.77%) |
| occurrences (all)           | 0               | 1               | 1               |
| Ear discomfort              |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)           | 0               | 1               | 0               |
| Ear disorder                |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)           | 0               | 1               | 0               |

|                                                                                  |                        |                        |                      |
|----------------------------------------------------------------------------------|------------------------|------------------------|----------------------|
| Excessive cerumen production<br>subjects affected / exposed<br>occurrences (all) | 0 / 262 (0.00%)<br>0   | 1 / 307 (0.33%)<br>1   | 0 / 130 (0.00%)<br>0 |
| Presbycusis<br>subjects affected / exposed<br>occurrences (all)                  | 0 / 262 (0.00%)<br>0   | 1 / 307 (0.33%)<br>1   | 0 / 130 (0.00%)<br>0 |
| Eye disorders                                                                    |                        |                        |                      |
| Vision blurred<br>subjects affected / exposed<br>occurrences (all)               | 14 / 262 (5.34%)<br>15 | 12 / 307 (3.91%)<br>15 | 4 / 130 (3.08%)<br>5 |
| Dry eye<br>subjects affected / exposed<br>occurrences (all)                      | 5 / 262 (1.91%)<br>6   | 0 / 307 (0.00%)<br>0   | 0 / 130 (0.00%)<br>0 |
| Diplopia<br>subjects affected / exposed<br>occurrences (all)                     | 3 / 262 (1.15%)<br>3   | 0 / 307 (0.00%)<br>0   | 0 / 130 (0.00%)<br>0 |
| Lacrimation increased<br>subjects affected / exposed<br>occurrences (all)        | 3 / 262 (1.15%)<br>3   | 5 / 307 (1.63%)<br>6   | 1 / 130 (0.77%)<br>1 |
| Eyelid ptosis<br>subjects affected / exposed<br>occurrences (all)                | 2 / 262 (0.76%)<br>3   | 1 / 307 (0.33%)<br>1   | 0 / 130 (0.00%)<br>0 |
| Vitreous floaters<br>subjects affected / exposed<br>occurrences (all)            | 2 / 262 (0.76%)<br>2   | 2 / 307 (0.65%)<br>2   | 1 / 130 (0.77%)<br>1 |
| Cataract<br>subjects affected / exposed<br>occurrences (all)                     | 1 / 262 (0.38%)<br>1   | 1 / 307 (0.33%)<br>1   | 1 / 130 (0.77%)<br>1 |
| Conjunctival haemorrhage<br>subjects affected / exposed<br>occurrences (all)     | 1 / 262 (0.38%)<br>1   | 1 / 307 (0.33%)<br>1   | 1 / 130 (0.77%)<br>1 |
| Conjunctival hyperaemia<br>subjects affected / exposed<br>occurrences (all)      | 1 / 262 (0.38%)<br>1   | 2 / 307 (0.65%)<br>2   | 0 / 130 (0.00%)<br>0 |
| Conjunctival oedema                                                              |                        |                        |                      |

|                             |                 |                 |                 |
|-----------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)           | 1               | 0               | 0               |
| Erythema of eyelid          |                 |                 |                 |
| subjects affected / exposed | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)           | 1               | 0               | 0               |
| Eye discharge               |                 |                 |                 |
| subjects affected / exposed | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)           | 1               | 0               | 0               |
| Eye disorder                |                 |                 |                 |
| subjects affected / exposed | 1 / 262 (0.38%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)           | 1               | 1               | 0               |
| Eye inflammation            |                 |                 |                 |
| subjects affected / exposed | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)           | 1               | 0               | 0               |
| Eye pain                    |                 |                 |                 |
| subjects affected / exposed | 1 / 262 (0.38%) | 1 / 307 (0.33%) | 2 / 130 (1.54%) |
| occurrences (all)           | 1               | 1               | 2               |
| Eye pruritus                |                 |                 |                 |
| subjects affected / exposed | 1 / 262 (0.38%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)           | 1               | 1               | 0               |
| Eyelid oedema               |                 |                 |                 |
| subjects affected / exposed | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)           | 1               | 0               | 0               |
| Ocular discomfort           |                 |                 |                 |
| subjects affected / exposed | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)           | 1               | 0               | 0               |
| Periorbital oedema          |                 |                 |                 |
| subjects affected / exposed | 1 / 262 (0.38%) | 1 / 307 (0.33%) | 1 / 130 (0.77%) |
| occurrences (all)           | 1               | 1               | 1               |
| Retinal haemorrhage         |                 |                 |                 |
| subjects affected / exposed | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)           | 1               | 0               | 0               |
| Visual acuity reduced       |                 |                 |                 |
| subjects affected / exposed | 1 / 262 (0.38%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)           | 2               | 1               | 0               |
| Asthenopia                  |                 |                 |                 |

|                             |                 |                 |                 |
|-----------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)           | 0               | 1               | 0               |
| Blepharitis                 |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)           | 0               | 1               | 0               |
| Conjunctivitis allergic     |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)           | 0               | 1               | 0               |
| Eye haemorrhage             |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 0 / 307 (0.00%) | 1 / 130 (0.77%) |
| occurrences (all)           | 0               | 0               | 1               |
| Eye irritation              |                 |                 |                 |
| subjects affected / exposed | 1 / 262 (0.38%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)           | 1               | 2               | 0               |
| Eye swelling                |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)           | 0               | 1               | 0               |
| Glaucoma                    |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)           | 0               | 1               | 0               |
| Hypermetropia               |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)           | 0               | 1               | 0               |
| Mydriasis                   |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 0 / 307 (0.00%) | 1 / 130 (0.77%) |
| occurrences (all)           | 0               | 0               | 1               |
| Ocular hyperaemia           |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)           | 0               | 1               | 0               |
| Photopsia                   |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)           | 0               | 1               | 0               |
| Retinal detachment          |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 0 / 307 (0.00%) | 1 / 130 (0.77%) |
| occurrences (all)           | 0               | 0               | 1               |
| Retinal tear                |                 |                 |                 |

|                                  |                    |                    |                   |
|----------------------------------|--------------------|--------------------|-------------------|
| subjects affected / exposed      | 0 / 262 (0.00%)    | 0 / 307 (0.00%)    | 1 / 130 (0.77%)   |
| occurrences (all)                | 0                  | 0                  | 1                 |
| Scleral hyperaemia               |                    |                    |                   |
| subjects affected / exposed      | 0 / 262 (0.00%)    | 1 / 307 (0.33%)    | 0 / 130 (0.00%)   |
| occurrences (all)                | 0                  | 1                  | 0                 |
| Visual impairment                |                    |                    |                   |
| subjects affected / exposed      | 0 / 262 (0.00%)    | 3 / 307 (0.98%)    | 2 / 130 (1.54%)   |
| occurrences (all)                | 0                  | 3                  | 4                 |
| Xerophthalmia                    |                    |                    |                   |
| subjects affected / exposed      | 0 / 262 (0.00%)    | 1 / 307 (0.33%)    | 0 / 130 (0.00%)   |
| occurrences (all)                | 0                  | 1                  | 0                 |
| Gastrointestinal disorders       |                    |                    |                   |
| Diarrhoea                        |                    |                    |                   |
| subjects affected / exposed      | 114 / 262 (43.51%) | 163 / 307 (53.09%) | 62 / 130 (47.69%) |
| occurrences (all)                | 252                | 372                | 96                |
| Nausea                           |                    |                    |                   |
| subjects affected / exposed      | 104 / 262 (39.69%) | 120 / 307 (39.09%) | 56 / 130 (43.08%) |
| occurrences (all)                | 144                | 177                | 79                |
| Vomiting                         |                    |                    |                   |
| subjects affected / exposed      | 39 / 262 (14.89%)  | 65 / 307 (21.17%)  | 35 / 130 (26.92%) |
| occurrences (all)                | 58                 | 86                 | 56                |
| Constipation                     |                    |                    |                   |
| subjects affected / exposed      | 30 / 262 (11.45%)  | 29 / 307 (9.45%)   | 19 / 130 (14.62%) |
| occurrences (all)                | 32                 | 37                 | 21                |
| Abdominal pain                   |                    |                    |                   |
| subjects affected / exposed      | 28 / 262 (10.69%)  | 37 / 307 (12.05%)  | 17 / 130 (13.08%) |
| occurrences (all)                | 37                 | 51                 | 18                |
| Gastrooesophageal reflux disease |                    |                    |                   |
| subjects affected / exposed      | 17 / 262 (6.49%)   | 15 / 307 (4.89%)   | 4 / 130 (3.08%)   |
| occurrences (all)                | 17                 | 16                 | 4                 |
| Dyspepsia                        |                    |                    |                   |
| subjects affected / exposed      | 12 / 262 (4.58%)   | 26 / 307 (8.47%)   | 15 / 130 (11.54%) |
| occurrences (all)                | 12                 | 30                 | 18                |
| Abdominal pain upper             |                    |                    |                   |
| subjects affected / exposed      | 10 / 262 (3.82%)   | 18 / 307 (5.86%)   | 1 / 130 (0.77%)   |
| occurrences (all)                | 11                 | 30                 | 1                 |

|                             |                  |                  |                 |
|-----------------------------|------------------|------------------|-----------------|
| Colitis                     |                  |                  |                 |
| subjects affected / exposed | 10 / 262 (3.82%) | 5 / 307 (1.63%)  | 1 / 130 (0.77%) |
| occurrences (all)           | 14               | 6                | 1               |
| Abdominal distension        |                  |                  |                 |
| subjects affected / exposed | 9 / 262 (3.44%)  | 20 / 307 (6.51%) | 7 / 130 (5.38%) |
| occurrences (all)           | 10               | 21               | 8               |
| Abdominal discomfort        |                  |                  |                 |
| subjects affected / exposed | 8 / 262 (3.05%)  | 7 / 307 (2.28%)  | 2 / 130 (1.54%) |
| occurrences (all)           | 9                | 7                | 3               |
| Flatulence                  |                  |                  |                 |
| subjects affected / exposed | 8 / 262 (3.05%)  | 14 / 307 (4.56%) | 2 / 130 (1.54%) |
| occurrences (all)           | 9                | 15               | 3               |
| Dry mouth                   |                  |                  |                 |
| subjects affected / exposed | 6 / 262 (2.29%)  | 5 / 307 (1.63%)  | 1 / 130 (0.77%) |
| occurrences (all)           | 6                | 5                | 1               |
| Dysphagia                   |                  |                  |                 |
| subjects affected / exposed | 6 / 262 (2.29%)  | 7 / 307 (2.28%)  | 5 / 130 (3.85%) |
| occurrences (all)           | 7                | 8                | 5               |
| Stomatitis                  |                  |                  |                 |
| subjects affected / exposed | 6 / 262 (2.29%)  | 15 / 307 (4.89%) | 7 / 130 (5.38%) |
| occurrences (all)           | 7                | 16               | 9               |
| Anal incontinence           |                  |                  |                 |
| subjects affected / exposed | 5 / 262 (1.91%)  | 2 / 307 (0.65%)  | 0 / 130 (0.00%) |
| occurrences (all)           | 5                | 2                | 0               |
| Haemorrhoids                |                  |                  |                 |
| subjects affected / exposed | 5 / 262 (1.91%)  | 2 / 307 (0.65%)  | 1 / 130 (0.77%) |
| occurrences (all)           | 5                | 2                | 2               |
| Inguinal hernia             |                  |                  |                 |
| subjects affected / exposed | 4 / 262 (1.53%)  | 2 / 307 (0.65%)  | 0 / 130 (0.00%) |
| occurrences (all)           | 4                | 2                | 0               |
| Oral pain                   |                  |                  |                 |
| subjects affected / exposed | 4 / 262 (1.53%)  | 6 / 307 (1.95%)  | 2 / 130 (1.54%) |
| occurrences (all)           | 4                | 7                | 2               |
| Abdominal pain lower        |                  |                  |                 |
| subjects affected / exposed | 3 / 262 (1.15%)  | 3 / 307 (0.98%)  | 1 / 130 (0.77%) |
| occurrences (all)           | 3                | 4                | 1               |

|                             |                 |                 |                 |
|-----------------------------|-----------------|-----------------|-----------------|
| Ascites                     |                 |                 |                 |
| subjects affected / exposed | 3 / 262 (1.15%) | 2 / 307 (0.65%) | 2 / 130 (1.54%) |
| occurrences (all)           | 5               | 2               | 3               |
| Gastritis                   |                 |                 |                 |
| subjects affected / exposed | 3 / 262 (1.15%) | 3 / 307 (0.98%) | 0 / 130 (0.00%) |
| occurrences (all)           | 3               | 3               | 0               |
| Toothache                   |                 |                 |                 |
| subjects affected / exposed | 3 / 262 (1.15%) | 4 / 307 (1.30%) | 0 / 130 (0.00%) |
| occurrences (all)           | 4               | 4               | 0               |
| Eructation                  |                 |                 |                 |
| subjects affected / exposed | 2 / 262 (0.76%) | 2 / 307 (0.65%) | 0 / 130 (0.00%) |
| occurrences (all)           | 2               | 2               | 0               |
| Haemorrhoidal haemorrhage   |                 |                 |                 |
| subjects affected / exposed | 2 / 262 (0.76%) | 2 / 307 (0.65%) | 2 / 130 (1.54%) |
| occurrences (all)           | 2               | 2               | 2               |
| Mouth ulceration            |                 |                 |                 |
| subjects affected / exposed | 2 / 262 (0.76%) | 0 / 307 (0.00%) | 3 / 130 (2.31%) |
| occurrences (all)           | 2               | 0               | 3               |
| Proctalgia                  |                 |                 |                 |
| subjects affected / exposed | 2 / 262 (0.76%) | 1 / 307 (0.33%) | 1 / 130 (0.77%) |
| occurrences (all)           | 2               | 1               | 1               |
| Salivary hypersecretion     |                 |                 |                 |
| subjects affected / exposed | 2 / 262 (0.76%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)           | 2               | 0               | 0               |
| Abdominal hernia            |                 |                 |                 |
| subjects affected / exposed | 1 / 262 (0.38%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)           | 1               | 1               | 0               |
| Abdominal rigidity          |                 |                 |                 |
| subjects affected / exposed | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)           | 1               | 0               | 0               |
| Anal polyp                  |                 |                 |                 |
| subjects affected / exposed | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)           | 1               | 0               | 0               |
| Barrett's oesophagus        |                 |                 |                 |
| subjects affected / exposed | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 1 / 130 (0.77%) |
| occurrences (all)           | 1               | 0               | 1               |

|                                  |                 |                 |                 |
|----------------------------------|-----------------|-----------------|-----------------|
| Chapped lips                     |                 |                 |                 |
| subjects affected / exposed      | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)                | 1               | 0               | 0               |
| Diverticulum                     |                 |                 |                 |
| subjects affected / exposed      | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)                | 1               | 0               | 0               |
| Duodenitis                       |                 |                 |                 |
| subjects affected / exposed      | 1 / 262 (0.38%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)                | 1               | 1               | 0               |
| Enterocolitis                    |                 |                 |                 |
| subjects affected / exposed      | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)                | 3               | 0               | 0               |
| Epigastric discomfort            |                 |                 |                 |
| subjects affected / exposed      | 1 / 262 (0.38%) | 1 / 307 (0.33%) | 3 / 130 (2.31%) |
| occurrences (all)                | 1               | 1               | 3               |
| Faeces discoloured               |                 |                 |                 |
| subjects affected / exposed      | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)                | 1               | 0               | 0               |
| Gastrointestinal pain            |                 |                 |                 |
| subjects affected / exposed      | 1 / 262 (0.38%) | 1 / 307 (0.33%) | 1 / 130 (0.77%) |
| occurrences (all)                | 1               | 1               | 1               |
| Gastrointestinal sounds abnormal |                 |                 |                 |
| subjects affected / exposed      | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)                | 1               | 0               | 0               |
| Haematochezia                    |                 |                 |                 |
| subjects affected / exposed      | 1 / 262 (0.38%) | 1 / 307 (0.33%) | 1 / 130 (0.77%) |
| occurrences (all)                | 1               | 1               | 1               |
| Hiatus hernia                    |                 |                 |                 |
| subjects affected / exposed      | 1 / 262 (0.38%) | 3 / 307 (0.98%) | 0 / 130 (0.00%) |
| occurrences (all)                | 1               | 3               | 0               |
| Large intestine polyp            |                 |                 |                 |
| subjects affected / exposed      | 1 / 262 (0.38%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)                | 1               | 1               | 0               |
| Leukoplakia oral                 |                 |                 |                 |
| subjects affected / exposed      | 1 / 262 (0.38%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)                | 1               | 1               | 0               |

|                             |                 |                 |                 |
|-----------------------------|-----------------|-----------------|-----------------|
| Lip blister                 |                 |                 |                 |
| subjects affected / exposed | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)           | 1               | 0               | 0               |
| Mouth haemorrhage           |                 |                 |                 |
| subjects affected / exposed | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)           | 1               | 0               | 0               |
| Oesophagitis                |                 |                 |                 |
| subjects affected / exposed | 1 / 262 (0.38%) | 2 / 307 (0.65%) | 0 / 130 (0.00%) |
| occurrences (all)           | 1               | 2               | 0               |
| Oral dysaesthesia           |                 |                 |                 |
| subjects affected / exposed | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)           | 1               | 0               | 0               |
| Oral mucosal eruption       |                 |                 |                 |
| subjects affected / exposed | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)           | 1               | 0               | 0               |
| Pancreatitis                |                 |                 |                 |
| subjects affected / exposed | 1 / 262 (0.38%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)           | 1               | 1               | 0               |
| Parotid gland enlargement   |                 |                 |                 |
| subjects affected / exposed | 1 / 262 (0.38%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)           | 1               | 1               | 0               |
| Proctitis                   |                 |                 |                 |
| subjects affected / exposed | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)           | 1               | 0               | 0               |
| Rectal haemorrhage          |                 |                 |                 |
| subjects affected / exposed | 1 / 262 (0.38%) | 2 / 307 (0.65%) | 0 / 130 (0.00%) |
| occurrences (all)           | 1               | 2               | 0               |
| Salivary gland pain         |                 |                 |                 |
| subjects affected / exposed | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)           | 1               | 0               | 0               |
| Tongue coated               |                 |                 |                 |
| subjects affected / exposed | 1 / 262 (0.38%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)           | 1               | 1               | 0               |
| Tongue disorder             |                 |                 |                 |
| subjects affected / exposed | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)           | 1               | 0               | 0               |

|                             |                 |                 |                 |
|-----------------------------|-----------------|-----------------|-----------------|
| Umbilical hernia            |                 |                 |                 |
| subjects affected / exposed | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)           | 1               | 0               | 0               |
| Abdominal adhesions         |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)           | 0               | 1               | 0               |
| Abdominal mass              |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 0 / 307 (0.00%) | 1 / 130 (0.77%) |
| occurrences (all)           | 0               | 0               | 1               |
| Abdominal tenderness        |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 1 / 130 (0.77%) |
| occurrences (all)           | 0               | 1               | 1               |
| Abnormal faeces             |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)           | 0               | 1               | 0               |
| Aphthous ulcer              |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)           | 0               | 2               | 0               |
| Apical granuloma            |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)           | 0               | 1               | 0               |
| Autoimmune enteropathy      |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)           | 0               | 1               | 0               |
| Breath odour                |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)           | 0               | 1               | 0               |
| Chronic gastritis           |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 2 / 307 (0.65%) | 0 / 130 (0.00%) |
| occurrences (all)           | 0               | 2               | 0               |
| Colitis microscopic         |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)           | 0               | 1               | 0               |
| Defaecation urgency         |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)           | 0               | 1               | 0               |

|                                           |                 |                 |                 |
|-------------------------------------------|-----------------|-----------------|-----------------|
| Diverticulum intestinal                   |                 |                 |                 |
| subjects affected / exposed               | 0 / 262 (0.00%) | 2 / 307 (0.65%) | 0 / 130 (0.00%) |
| occurrences (all)                         | 0               | 3               | 0               |
| Faecal vomiting                           |                 |                 |                 |
| subjects affected / exposed               | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)                         | 0               | 1               | 0               |
| Faeces soft                               |                 |                 |                 |
| subjects affected / exposed               | 0 / 262 (0.00%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)                         | 0               | 0               | 0               |
| Frequent bowel movements                  |                 |                 |                 |
| subjects affected / exposed               | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)                         | 0               | 1               | 0               |
| Gastric disorder                          |                 |                 |                 |
| subjects affected / exposed               | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)                         | 0               | 1               | 0               |
| Gastric mucosa erythema                   |                 |                 |                 |
| subjects affected / exposed               | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)                         | 0               | 1               | 0               |
| Gastric ulcer                             |                 |                 |                 |
| subjects affected / exposed               | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)                         | 0               | 1               | 0               |
| Gastritis haemorrhagic                    |                 |                 |                 |
| subjects affected / exposed               | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)                         | 0               | 1               | 0               |
| Gastrooesophageal sphincter insufficiency |                 |                 |                 |
| subjects affected / exposed               | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)                         | 0               | 1               | 0               |
| Gingival bleeding                         |                 |                 |                 |
| subjects affected / exposed               | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)                         | 0               | 1               | 0               |
| Gingival pain                             |                 |                 |                 |
| subjects affected / exposed               | 0 / 262 (0.00%) | 0 / 307 (0.00%) | 1 / 130 (0.77%) |
| occurrences (all)                         | 0               | 0               | 1               |
| Haematemesis                              |                 |                 |                 |

|                             |                 |                 |                 |
|-----------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)           | 0               | 1               | 0               |
| Hypoaesthesia oral          |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)           | 0               | 1               | 0               |
| Ileus                       |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)           | 0               | 1               | 0               |
| Impaired gastric emptying   |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)           | 0               | 1               | 0               |
| Intra-abdominal haematoma   |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 0 / 307 (0.00%) | 1 / 130 (0.77%) |
| occurrences (all)           | 0               | 0               | 1               |
| Irritable bowel syndrome    |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)           | 0               | 1               | 0               |
| Large intestinal ulcer      |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)           | 0               | 1               | 0               |
| Lip exfoliation             |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 0 / 307 (0.00%) | 1 / 130 (0.77%) |
| occurrences (all)           | 0               | 0               | 1               |
| Melaena                     |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)           | 0               | 1               | 0               |
| Mesenteric vein thrombosis  |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 0 / 307 (0.00%) | 1 / 130 (0.77%) |
| occurrences (all)           | 0               | 0               | 1               |
| Neutropenic colitis         |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 0 / 307 (0.00%) | 1 / 130 (0.77%) |
| occurrences (all)           | 0               | 0               | 4               |
| Odynophagia                 |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 2 / 307 (0.65%) | 0 / 130 (0.00%) |
| occurrences (all)           | 0               | 2               | 0               |
| Oedematous pancreatitis     |                 |                 |                 |

|                             |                 |                 |                 |
|-----------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)           | 0               | 1               | 0               |
| Oesophageal stenosis        |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)           | 0               | 1               | 0               |
| Oral disorder               |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)           | 0               | 1               | 0               |
| Oral mucosal blistering     |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)           | 0               | 1               | 0               |
| Palatal disorder            |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)           | 0               | 1               | 0               |
| Pancreatitis acute          |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)           | 0               | 1               | 0               |
| Paraesthesia oral           |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 3 / 307 (0.98%) | 0 / 130 (0.00%) |
| occurrences (all)           | 0               | 4               | 0               |
| Periodontal disease         |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 0 / 307 (0.00%) | 1 / 130 (0.77%) |
| occurrences (all)           | 0               | 0               | 1               |
| Poor dental condition       |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)           | 0               | 1               | 0               |
| Reflux gastritis            |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)           | 0               | 1               | 0               |
| Stomatitis necrotising      |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)           | 0               | 1               | 0               |
| Tongue ulceration           |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 3 / 307 (0.98%) | 0 / 130 (0.00%) |
| occurrences (all)           | 0               | 4               | 0               |
| Varices oesophageal         |                 |                 |                 |

|                                                  |                      |                      |                      |
|--------------------------------------------------|----------------------|----------------------|----------------------|
| subjects affected / exposed<br>occurrences (all) | 0 / 262 (0.00%)<br>0 | 1 / 307 (0.33%)<br>1 | 0 / 130 (0.00%)<br>0 |
| Skin and subcutaneous tissue disorders           |                      |                      |                      |
| Rash                                             |                      |                      |                      |
| subjects affected / exposed                      | 23 / 262 (8.78%)     | 27 / 307 (8.79%)     | 16 / 130 (12.31%)    |
| occurrences (all)                                | 24                   | 30                   | 21                   |
| Pruritus                                         |                      |                      |                      |
| subjects affected / exposed                      | 20 / 262 (7.63%)     | 14 / 307 (4.56%)     | 12 / 130 (9.23%)     |
| occurrences (all)                                | 24                   | 19                   | 16                   |
| Erythema                                         |                      |                      |                      |
| subjects affected / exposed                      | 9 / 262 (3.44%)      | 8 / 307 (2.61%)      | 3 / 130 (2.31%)      |
| occurrences (all)                                | 15                   | 12                   | 3                    |
| Alopecia                                         |                      |                      |                      |
| subjects affected / exposed                      | 8 / 262 (3.05%)      | 10 / 307 (3.26%)     | 0 / 130 (0.00%)      |
| occurrences (all)                                | 8                    | 10                   | 0                    |
| Hyperhidrosis                                    |                      |                      |                      |
| subjects affected / exposed                      | 8 / 262 (3.05%)      | 13 / 307 (4.23%)     | 2 / 130 (1.54%)      |
| occurrences (all)                                | 8                    | 14                   | 2                    |
| Night sweats                                     |                      |                      |                      |
| subjects affected / exposed                      | 8 / 262 (3.05%)      | 22 / 307 (7.17%)     | 5 / 130 (3.85%)      |
| occurrences (all)                                | 9                    | 25                   | 5                    |
| Rash maculo-papular                              |                      |                      |                      |
| subjects affected / exposed                      | 8 / 262 (3.05%)      | 11 / 307 (3.58%)     | 9 / 130 (6.92%)      |
| occurrences (all)                                | 12                   | 13                   | 13                   |
| Dry skin                                         |                      |                      |                      |
| subjects affected / exposed                      | 7 / 262 (2.67%)      | 10 / 307 (3.26%)     | 5 / 130 (3.85%)      |
| occurrences (all)                                | 8                    | 11                   | 6                    |
| Rash pruritic                                    |                      |                      |                      |
| subjects affected / exposed                      | 4 / 262 (1.53%)      | 2 / 307 (0.65%)      | 4 / 130 (3.08%)      |
| occurrences (all)                                | 7                    | 2                    | 4                    |
| Skin mass                                        |                      |                      |                      |
| subjects affected / exposed                      | 4 / 262 (1.53%)      | 3 / 307 (0.98%)      | 0 / 130 (0.00%)      |
| occurrences (all)                                | 4                    | 3                    | 0                    |
| Ecchymosis                                       |                      |                      |                      |
| subjects affected / exposed                      | 3 / 262 (1.15%)      | 0 / 307 (0.00%)      | 1 / 130 (0.77%)      |
| occurrences (all)                                | 4                    | 0                    | 1                    |

|                             |                 |                 |                 |
|-----------------------------|-----------------|-----------------|-----------------|
| Skin ulcer                  |                 |                 |                 |
| subjects affected / exposed | 3 / 262 (1.15%) | 2 / 307 (0.65%) | 2 / 130 (1.54%) |
| occurrences (all)           | 3               | 3               | 2               |
| Actinic keratosis           |                 |                 |                 |
| subjects affected / exposed | 2 / 262 (0.76%) | 1 / 307 (0.33%) | 1 / 130 (0.77%) |
| occurrences (all)           | 2               | 1               | 1               |
| Dermatitis                  |                 |                 |                 |
| subjects affected / exposed | 2 / 262 (0.76%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)           | 2               | 1               | 0               |
| Pain of skin                |                 |                 |                 |
| subjects affected / exposed | 2 / 262 (0.76%) | 0 / 307 (0.00%) | 1 / 130 (0.77%) |
| occurrences (all)           | 2               | 0               | 1               |
| Urticaria                   |                 |                 |                 |
| subjects affected / exposed | 2 / 262 (0.76%) | 2 / 307 (0.65%) | 0 / 130 (0.00%) |
| occurrences (all)           | 3               | 4               | 0               |
| Angioedema                  |                 |                 |                 |
| subjects affected / exposed | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)           | 2               | 0               | 0               |
| Blister                     |                 |                 |                 |
| subjects affected / exposed | 1 / 262 (0.38%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)           | 1               | 1               | 0               |
| Decubitus ulcer             |                 |                 |                 |
| subjects affected / exposed | 1 / 262 (0.38%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)           | 1               | 1               | 0               |
| Dermatitis atopic           |                 |                 |                 |
| subjects affected / exposed | 1 / 262 (0.38%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)           | 1               | 1               | 0               |
| Eczema asteatotic           |                 |                 |                 |
| subjects affected / exposed | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)           | 1               | 0               | 0               |
| Exfoliative rash            |                 |                 |                 |
| subjects affected / exposed | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)           | 1               | 0               | 0               |
| Hyperkeratosis              |                 |                 |                 |
| subjects affected / exposed | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)           | 1               | 0               | 0               |

|                             |                 |                 |                 |
|-----------------------------|-----------------|-----------------|-----------------|
| Hypersensitivity vasculitis |                 |                 |                 |
| subjects affected / exposed | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)           | 1               | 0               | 0               |
| Onychoclasia                |                 |                 |                 |
| subjects affected / exposed | 1 / 262 (0.38%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)           | 1               | 1               | 0               |
| Psoriasis                   |                 |                 |                 |
| subjects affected / exposed | 1 / 262 (0.38%) | 3 / 307 (0.98%) | 0 / 130 (0.00%) |
| occurrences (all)           | 1               | 8               | 0               |
| Purpura                     |                 |                 |                 |
| subjects affected / exposed | 1 / 262 (0.38%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)           | 1               | 1               | 0               |
| Rash macular                |                 |                 |                 |
| subjects affected / exposed | 1 / 262 (0.38%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)           | 1               | 1               | 0               |
| Rosacea                     |                 |                 |                 |
| subjects affected / exposed | 1 / 262 (0.38%) | 2 / 307 (0.65%) | 0 / 130 (0.00%) |
| occurrences (all)           | 1               | 2               | 0               |
| Skin burning sensation      |                 |                 |                 |
| subjects affected / exposed | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)           | 1               | 0               | 0               |
| Skin discolouration         |                 |                 |                 |
| subjects affected / exposed | 1 / 262 (0.38%) | 1 / 307 (0.33%) | 2 / 130 (1.54%) |
| occurrences (all)           | 1               | 1               | 2               |
| Skin fissures               |                 |                 |                 |
| subjects affected / exposed | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)           | 1               | 0               | 0               |
| Skin irritation             |                 |                 |                 |
| subjects affected / exposed | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)           | 4               | 0               | 0               |
| Skin lesion                 |                 |                 |                 |
| subjects affected / exposed | 1 / 262 (0.38%) | 2 / 307 (0.65%) | 2 / 130 (1.54%) |
| occurrences (all)           | 1               | 2               | 2               |
| Skin tightness              |                 |                 |                 |
| subjects affected / exposed | 1 / 262 (0.38%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)           | 1               | 1               | 0               |

|                                             |                 |                 |                 |
|---------------------------------------------|-----------------|-----------------|-----------------|
| Stasis dermatitis                           |                 |                 |                 |
| subjects affected / exposed                 | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)                           | 1               | 0               | 0               |
| Cold sweat                                  |                 |                 |                 |
| subjects affected / exposed                 | 0 / 262 (0.00%) | 0 / 307 (0.00%) | 1 / 130 (0.77%) |
| occurrences (all)                           | 0               | 0               | 1               |
| Dermal cyst                                 |                 |                 |                 |
| subjects affected / exposed                 | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)                           | 0               | 1               | 0               |
| Dermatitis acneiform                        |                 |                 |                 |
| subjects affected / exposed                 | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 1 / 130 (0.77%) |
| occurrences (all)                           | 0               | 1               | 1               |
| Dermatitis bullous                          |                 |                 |                 |
| subjects affected / exposed                 | 0 / 262 (0.00%) | 0 / 307 (0.00%) | 1 / 130 (0.77%) |
| occurrences (all)                           | 0               | 0               | 1               |
| Dermatitis exfoliative generalised          |                 |                 |                 |
| subjects affected / exposed                 | 0 / 262 (0.00%) | 2 / 307 (0.65%) | 0 / 130 (0.00%) |
| occurrences (all)                           | 0               | 3               | 0               |
| Drug eruption                               |                 |                 |                 |
| subjects affected / exposed                 | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)                           | 0               | 1               | 0               |
| Eczema                                      |                 |                 |                 |
| subjects affected / exposed                 | 0 / 262 (0.00%) | 4 / 307 (1.30%) | 0 / 130 (0.00%) |
| occurrences (all)                           | 0               | 7               | 0               |
| Erythema multiforme                         |                 |                 |                 |
| subjects affected / exposed                 | 0 / 262 (0.00%) | 0 / 307 (0.00%) | 1 / 130 (0.77%) |
| occurrences (all)                           | 0               | 0               | 1               |
| Nail discolouration                         |                 |                 |                 |
| subjects affected / exposed                 | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)                           | 0               | 1               | 0               |
| Palmar-plantar erythrodysaesthesia syndrome |                 |                 |                 |
| subjects affected / exposed                 | 0 / 262 (0.00%) | 0 / 307 (0.00%) | 1 / 130 (0.77%) |
| occurrences (all)                           | 0               | 0               | 1               |
| Papule                                      |                 |                 |                 |

|                             |                 |                 |                 |
|-----------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)           | 0               | 1               | 0               |
| Photosensitivity reaction   |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 0 / 307 (0.00%) | 1 / 130 (0.77%) |
| occurrences (all)           | 0               | 0               | 1               |
| Purpura senile              |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)           | 0               | 1               | 0               |
| Rash erythematous           |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 2 / 307 (0.65%) | 0 / 130 (0.00%) |
| occurrences (all)           | 0               | 2               | 0               |
| Scab                        |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 0 / 307 (0.00%) | 1 / 130 (0.77%) |
| occurrences (all)           | 0               | 0               | 1               |
| Scar pain                   |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 0 / 307 (0.00%) | 1 / 130 (0.77%) |
| occurrences (all)           | 0               | 0               | 1               |
| Skin atrophy                |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)           | 0               | 1               | 0               |
| Skin discomfort             |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 0 / 307 (0.00%) | 1 / 130 (0.77%) |
| occurrences (all)           | 0               | 0               | 1               |
| Skin exfoliation            |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 4 / 307 (1.30%) | 0 / 130 (0.00%) |
| occurrences (all)           | 0               | 6               | 0               |
| Skin hypopigmentation       |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)           | 0               | 2               | 0               |
| Skin necrosis               |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 0 / 307 (0.00%) | 1 / 130 (0.77%) |
| occurrences (all)           | 0               | 0               | 1               |
| Skin plaque                 |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)           | 0               | 1               | 0               |
| Skin reaction               |                 |                 |                 |

|                             |                 |                 |                 |
|-----------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)           | 0               | 1               | 0               |
| Telangiectasia              |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)           | 0               | 1               | 0               |
| Renal and urinary disorders |                 |                 |                 |
| Pollakiuria                 |                 |                 |                 |
| subjects affected / exposed | 5 / 262 (1.91%) | 5 / 307 (1.63%) | 4 / 130 (3.08%) |
| occurrences (all)           | 5               | 5               | 4               |
| Acute kidney injury         |                 |                 |                 |
| subjects affected / exposed | 4 / 262 (1.53%) | 3 / 307 (0.98%) | 7 / 130 (5.38%) |
| occurrences (all)           | 6               | 3               | 9               |
| Haematuria                  |                 |                 |                 |
| subjects affected / exposed | 4 / 262 (1.53%) | 3 / 307 (0.98%) | 1 / 130 (0.77%) |
| occurrences (all)           | 5               | 3               | 1               |
| Dysuria                     |                 |                 |                 |
| subjects affected / exposed | 3 / 262 (1.15%) | 0 / 307 (0.00%) | 2 / 130 (1.54%) |
| occurrences (all)           | 4               | 0               | 2               |
| Chronic kidney disease      |                 |                 |                 |
| subjects affected / exposed | 2 / 262 (0.76%) | 2 / 307 (0.65%) | 1 / 130 (0.77%) |
| occurrences (all)           | 2               | 3               | 1               |
| Proteinuria                 |                 |                 |                 |
| subjects affected / exposed | 2 / 262 (0.76%) | 3 / 307 (0.98%) | 0 / 130 (0.00%) |
| occurrences (all)           | 2               | 3               | 0               |
| Calculus urinary            |                 |                 |                 |
| subjects affected / exposed | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)           | 1               | 0               | 0               |
| Micturition urgency         |                 |                 |                 |
| subjects affected / exposed | 1 / 262 (0.38%) | 1 / 307 (0.33%) | 1 / 130 (0.77%) |
| occurrences (all)           | 1               | 1               | 1               |
| Polyuria                    |                 |                 |                 |
| subjects affected / exposed | 1 / 262 (0.38%) | 2 / 307 (0.65%) | 0 / 130 (0.00%) |
| occurrences (all)           | 1               | 2               | 0               |
| Renal failure               |                 |                 |                 |
| subjects affected / exposed | 1 / 262 (0.38%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)           | 1               | 1               | 0               |

|                             |                 |                 |                 |
|-----------------------------|-----------------|-----------------|-----------------|
| Strangury                   |                 |                 |                 |
| subjects affected / exposed | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)           | 1               | 0               | 0               |
| Ureteric stenosis           |                 |                 |                 |
| subjects affected / exposed | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)           | 2               | 0               | 0               |
| Urinary hesitation          |                 |                 |                 |
| subjects affected / exposed | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)           | 1               | 0               | 0               |
| Urinary retention           |                 |                 |                 |
| subjects affected / exposed | 1 / 262 (0.38%) | 1 / 307 (0.33%) | 2 / 130 (1.54%) |
| occurrences (all)           | 1               | 1               | 2               |
| Urinary tract obstruction   |                 |                 |                 |
| subjects affected / exposed | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)           | 1               | 0               | 0               |
| Urine odour abnormal        |                 |                 |                 |
| subjects affected / exposed | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)           | 1               | 0               | 0               |
| Azotaemia                   |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)           | 0               | 1               | 0               |
| Bladder discomfort          |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 0 / 307 (0.00%) | 1 / 130 (0.77%) |
| occurrences (all)           | 0               | 0               | 1               |
| Haemorrhage urinary tract   |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 0 / 307 (0.00%) | 1 / 130 (0.77%) |
| occurrences (all)           | 0               | 0               | 1               |
| Hydronephrosis              |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 2 / 307 (0.65%) | 0 / 130 (0.00%) |
| occurrences (all)           | 0               | 2               | 0               |
| Hypertonic bladder          |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)           | 0               | 1               | 0               |
| Nephrolithiasis             |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 2 / 307 (0.65%) | 1 / 130 (0.77%) |
| occurrences (all)           | 0               | 2               | 1               |

|                                                 |                 |                 |                 |
|-------------------------------------------------|-----------------|-----------------|-----------------|
| Nephropathy                                     |                 |                 |                 |
| subjects affected / exposed                     | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)                               | 0               | 3               | 0               |
| Nocturia                                        |                 |                 |                 |
| subjects affected / exposed                     | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 1 / 130 (0.77%) |
| occurrences (all)                               | 0               | 1               | 1               |
| Renal pain                                      |                 |                 |                 |
| subjects affected / exposed                     | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)                               | 0               | 1               | 0               |
| Ureterolithiasis                                |                 |                 |                 |
| subjects affected / exposed                     | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)                               | 0               | 1               | 0               |
| Urinary incontinence                            |                 |                 |                 |
| subjects affected / exposed                     | 0 / 262 (0.00%) | 4 / 307 (1.30%) | 1 / 130 (0.77%) |
| occurrences (all)                               | 0               | 5               | 1               |
| Urinary tract pain                              |                 |                 |                 |
| subjects affected / exposed                     | 0 / 262 (0.00%) | 0 / 307 (0.00%) | 1 / 130 (0.77%) |
| occurrences (all)                               | 0               | 0               | 1               |
| Endocrine disorders                             |                 |                 |                 |
| Hypothyroidism                                  |                 |                 |                 |
| subjects affected / exposed                     | 2 / 262 (0.76%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)                               | 2               | 0               | 0               |
| Adrenal insufficiency                           |                 |                 |                 |
| subjects affected / exposed                     | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)                               | 1               | 0               | 0               |
| Hyperparathyroidism                             |                 |                 |                 |
| subjects affected / exposed                     | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)                               | 1               | 0               | 0               |
| Hypercalcaemia of malignancy                    |                 |                 |                 |
| subjects affected / exposed                     | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)                               | 0               | 1               | 0               |
| Hyperthyroidism                                 |                 |                 |                 |
| subjects affected / exposed                     | 0 / 262 (0.00%) | 3 / 307 (0.98%) | 0 / 130 (0.00%) |
| occurrences (all)                               | 0               | 3               | 0               |
| Musculoskeletal and connective tissue disorders |                 |                 |                 |

|                             |                   |                   |                   |
|-----------------------------|-------------------|-------------------|-------------------|
| Back pain                   |                   |                   |                   |
| subjects affected / exposed | 32 / 262 (12.21%) | 32 / 307 (10.42%) | 11 / 130 (8.46%)  |
| occurrences (all)           | 42                | 42                | 14                |
| Arthralgia                  |                   |                   |                   |
| subjects affected / exposed | 21 / 262 (8.02%)  | 34 / 307 (11.07%) | 17 / 130 (13.08%) |
| occurrences (all)           | 48                | 47                | 18                |
| Pain in extremity           |                   |                   |                   |
| subjects affected / exposed | 12 / 262 (4.58%)  | 25 / 307 (8.14%)  | 9 / 130 (6.92%)   |
| occurrences (all)           | 12                | 32                | 10                |
| Muscle spasms               |                   |                   |                   |
| subjects affected / exposed | 9 / 262 (3.44%)   | 19 / 307 (6.19%)  | 8 / 130 (6.15%)   |
| occurrences (all)           | 14                | 23                | 8                 |
| Muscular weakness           |                   |                   |                   |
| subjects affected / exposed | 8 / 262 (3.05%)   | 16 / 307 (5.21%)  | 8 / 130 (6.15%)   |
| occurrences (all)           | 8                 | 20                | 9                 |
| Flank pain                  |                   |                   |                   |
| subjects affected / exposed | 6 / 262 (2.29%)   | 11 / 307 (3.58%)  | 2 / 130 (1.54%)   |
| occurrences (all)           | 8                 | 12                | 2                 |
| Groin pain                  |                   |                   |                   |
| subjects affected / exposed | 5 / 262 (1.91%)   | 10 / 307 (3.26%)  | 3 / 130 (2.31%)   |
| occurrences (all)           | 5                 | 10                | 3                 |
| Musculoskeletal pain        |                   |                   |                   |
| subjects affected / exposed | 5 / 262 (1.91%)   | 13 / 307 (4.23%)  | 3 / 130 (2.31%)   |
| occurrences (all)           | 5                 | 19                | 4                 |
| Joint swelling              |                   |                   |                   |
| subjects affected / exposed | 4 / 262 (1.53%)   | 2 / 307 (0.65%)   | 0 / 130 (0.00%)   |
| occurrences (all)           | 4                 | 2                 | 0                 |
| Bone pain                   |                   |                   |                   |
| subjects affected / exposed | 3 / 262 (1.15%)   | 4 / 307 (1.30%)   | 8 / 130 (6.15%)   |
| occurrences (all)           | 4                 | 7                 | 8                 |
| Musculoskeletal discomfort  |                   |                   |                   |
| subjects affected / exposed | 3 / 262 (1.15%)   | 1 / 307 (0.33%)   | 0 / 130 (0.00%)   |
| occurrences (all)           | 4                 | 1                 | 0                 |
| Arthritis                   |                   |                   |                   |
| subjects affected / exposed | 2 / 262 (0.76%)   | 3 / 307 (0.98%)   | 1 / 130 (0.77%)   |
| occurrences (all)           | 2                 | 4                 | 1                 |

|                                |                 |                 |                 |
|--------------------------------|-----------------|-----------------|-----------------|
| Muscle tightness               |                 |                 |                 |
| subjects affected / exposed    | 2 / 262 (0.76%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)              | 2               | 1               | 0               |
| Musculoskeletal chest pain     |                 |                 |                 |
| subjects affected / exposed    | 2 / 262 (0.76%) | 4 / 307 (1.30%) | 2 / 130 (1.54%) |
| occurrences (all)              | 2               | 5               | 2               |
| Osteoporosis                   |                 |                 |                 |
| subjects affected / exposed    | 2 / 262 (0.76%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)              | 2               | 0               | 0               |
| Pain in jaw                    |                 |                 |                 |
| subjects affected / exposed    | 2 / 262 (0.76%) | 3 / 307 (0.98%) | 0 / 130 (0.00%) |
| occurrences (all)              | 3               | 3               | 0               |
| Axillary mass                  |                 |                 |                 |
| subjects affected / exposed    | 1 / 262 (0.38%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)              | 1               | 1               | 0               |
| Intervertebral disc protrusion |                 |                 |                 |
| subjects affected / exposed    | 1 / 262 (0.38%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)              | 1               | 1               | 0               |
| Joint stiffness                |                 |                 |                 |
| subjects affected / exposed    | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)              | 1               | 0               | 0               |
| Osteoarthritis                 |                 |                 |                 |
| subjects affected / exposed    | 1 / 262 (0.38%) | 2 / 307 (0.65%) | 1 / 130 (0.77%) |
| occurrences (all)              | 1               | 2               | 1               |
| Periarthritis                  |                 |                 |                 |
| subjects affected / exposed    | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)              | 1               | 0               | 0               |
| Psoriatic arthropathy          |                 |                 |                 |
| subjects affected / exposed    | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)              | 1               | 0               | 0               |
| Rheumatoid arthritis           |                 |                 |                 |
| subjects affected / exposed    | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)              | 1               | 0               | 0               |
| Rotator cuff syndrome          |                 |                 |                 |
| subjects affected / exposed    | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)              | 1               | 0               | 0               |

|                                 |                 |                 |                 |
|---------------------------------|-----------------|-----------------|-----------------|
| Spinal osteoarthritis           |                 |                 |                 |
| subjects affected / exposed     | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)               | 1               | 0               | 0               |
| Spinal pain                     |                 |                 |                 |
| subjects affected / exposed     | 1 / 262 (0.38%) | 6 / 307 (1.95%) | 0 / 130 (0.00%) |
| occurrences (all)               | 2               | 12              | 0               |
| Trigger finger                  |                 |                 |                 |
| subjects affected / exposed     | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)               | 1               | 0               | 0               |
| Bursitis                        |                 |                 |                 |
| subjects affected / exposed     | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)               | 0               | 1               | 0               |
| Coccydynia                      |                 |                 |                 |
| subjects affected / exposed     | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)               | 0               | 1               | 0               |
| Gouty arthritis                 |                 |                 |                 |
| subjects affected / exposed     | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)               | 0               | 1               | 0               |
| Joint range of motion decreased |                 |                 |                 |
| subjects affected / exposed     | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)               | 0               | 1               | 0               |
| Limb discomfort                 |                 |                 |                 |
| subjects affected / exposed     | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)               | 0               | 1               | 0               |
| Muscle fatigue                  |                 |                 |                 |
| subjects affected / exposed     | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)               | 0               | 1               | 0               |
| Muscle twitching                |                 |                 |                 |
| subjects affected / exposed     | 0 / 262 (0.00%) | 3 / 307 (0.98%) | 0 / 130 (0.00%) |
| occurrences (all)               | 0               | 3               | 0               |
| Musculoskeletal stiffness       |                 |                 |                 |
| subjects affected / exposed     | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 1 / 130 (0.77%) |
| occurrences (all)               | 0               | 1               | 1               |
| Rhabdomyolysis                  |                 |                 |                 |
| subjects affected / exposed     | 0 / 262 (0.00%) | 0 / 307 (0.00%) | 1 / 130 (0.77%) |
| occurrences (all)               | 0               | 0               | 1               |

|                                   |                  |                   |                  |
|-----------------------------------|------------------|-------------------|------------------|
| Synovial cyst                     |                  |                   |                  |
| subjects affected / exposed       | 0 / 262 (0.00%)  | 0 / 307 (0.00%)   | 1 / 130 (0.77%)  |
| occurrences (all)                 | 0                | 0                 | 1                |
| Tendon pain                       |                  |                   |                  |
| subjects affected / exposed       | 0 / 262 (0.00%)  | 0 / 307 (0.00%)   | 1 / 130 (0.77%)  |
| occurrences (all)                 | 0                | 0                 | 1                |
| Tendonitis                        |                  |                   |                  |
| subjects affected / exposed       | 0 / 262 (0.00%)  | 1 / 307 (0.33%)   | 0 / 130 (0.00%)  |
| occurrences (all)                 | 0                | 1                 | 0                |
| Infections and infestations       |                  |                   |                  |
| Urinary tract infection           |                  |                   |                  |
| subjects affected / exposed       | 17 / 262 (6.49%) | 22 / 307 (7.17%)  | 11 / 130 (8.46%) |
| occurrences (all)                 | 24               | 27                | 14               |
| Pneumonia                         |                  |                   |                  |
| subjects affected / exposed       | 12 / 262 (4.58%) | 10 / 307 (3.26%)  | 5 / 130 (3.85%)  |
| occurrences (all)                 | 19               | 11                | 5                |
| Upper respiratory tract infection |                  |                   |                  |
| subjects affected / exposed       | 12 / 262 (4.58%) | 42 / 307 (13.68%) | 7 / 130 (5.38%)  |
| occurrences (all)                 | 15               | 49                | 10               |
| COVID-19                          |                  |                   |                  |
| subjects affected / exposed       | 8 / 262 (3.05%)  | 9 / 307 (2.93%)   | 1 / 130 (0.77%)  |
| occurrences (all)                 | 8                | 11                | 1                |
| Sinusitis                         |                  |                   |                  |
| subjects affected / exposed       | 8 / 262 (3.05%)  | 8 / 307 (2.61%)   | 4 / 130 (3.08%)  |
| occurrences (all)                 | 8                | 13                | 5                |
| Oral candidiasis                  |                  |                   |                  |
| subjects affected / exposed       | 7 / 262 (2.67%)  | 2 / 307 (0.65%)   | 5 / 130 (3.85%)  |
| occurrences (all)                 | 10               | 2                 | 5                |
| Bronchitis                        |                  |                   |                  |
| subjects affected / exposed       | 5 / 262 (1.91%)  | 5 / 307 (1.63%)   | 5 / 130 (3.85%)  |
| occurrences (all)                 | 6                | 7                 | 10               |
| Candida infection                 |                  |                   |                  |
| subjects affected / exposed       | 5 / 262 (1.91%)  | 4 / 307 (1.30%)   | 1 / 130 (0.77%)  |
| occurrences (all)                 | 5                | 4                 | 1                |
| Nasopharyngitis                   |                  |                   |                  |

|                                        |                 |                 |                 |
|----------------------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed            | 5 / 262 (1.91%) | 7 / 307 (2.28%) | 2 / 130 (1.54%) |
| occurrences (all)                      | 5               | 11              | 2               |
| Respiratory tract infection            |                 |                 |                 |
| subjects affected / exposed            | 5 / 262 (1.91%) | 5 / 307 (1.63%) | 0 / 130 (0.00%) |
| occurrences (all)                      | 8               | 5               | 0               |
| Cytomegalovirus infection reactivation |                 |                 |                 |
| subjects affected / exposed            | 4 / 262 (1.53%) | 0 / 307 (0.00%) | 1 / 130 (0.77%) |
| occurrences (all)                      | 8               | 0               | 2               |
| Cytomegalovirus infection              |                 |                 |                 |
| subjects affected / exposed            | 3 / 262 (1.15%) | 0 / 307 (0.00%) | 1 / 130 (0.77%) |
| occurrences (all)                      | 3               | 0               | 1               |
| Folliculitis                           |                 |                 |                 |
| subjects affected / exposed            | 3 / 262 (1.15%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)                      | 4               | 0               | 0               |
| Gastroenteritis                        |                 |                 |                 |
| subjects affected / exposed            | 3 / 262 (1.15%) | 3 / 307 (0.98%) | 0 / 130 (0.00%) |
| occurrences (all)                      | 4               | 3               | 0               |
| Influenza                              |                 |                 |                 |
| subjects affected / exposed            | 3 / 262 (1.15%) | 5 / 307 (1.63%) | 1 / 130 (0.77%) |
| occurrences (all)                      | 3               | 7               | 1               |
| Lower respiratory tract infection      |                 |                 |                 |
| subjects affected / exposed            | 3 / 262 (1.15%) | 8 / 307 (2.61%) | 0 / 130 (0.00%) |
| occurrences (all)                      | 3               | 9               | 0               |
| Rhinitis                               |                 |                 |                 |
| subjects affected / exposed            | 3 / 262 (1.15%) | 3 / 307 (0.98%) | 0 / 130 (0.00%) |
| occurrences (all)                      | 7               | 3               | 0               |
| Sepsis                                 |                 |                 |                 |
| subjects affected / exposed            | 3 / 262 (1.15%) | 0 / 307 (0.00%) | 1 / 130 (0.77%) |
| occurrences (all)                      | 3               | 0               | 1               |
| Cellulitis                             |                 |                 |                 |
| subjects affected / exposed            | 2 / 262 (0.76%) | 4 / 307 (1.30%) | 2 / 130 (1.54%) |
| occurrences (all)                      | 2               | 7               | 3               |
| Chronic sinusitis                      |                 |                 |                 |
| subjects affected / exposed            | 2 / 262 (0.76%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)                      | 2               | 1               | 0               |

|                             |                 |                 |                 |
|-----------------------------|-----------------|-----------------|-----------------|
| Conjunctivitis              |                 |                 |                 |
| subjects affected / exposed | 2 / 262 (0.76%) | 1 / 307 (0.33%) | 1 / 130 (0.77%) |
| occurrences (all)           | 2               | 1               | 1               |
| Cystitis                    |                 |                 |                 |
| subjects affected / exposed | 2 / 262 (0.76%) | 1 / 307 (0.33%) | 1 / 130 (0.77%) |
| occurrences (all)           | 3               | 1               | 1               |
| Diverticulitis              |                 |                 |                 |
| subjects affected / exposed | 2 / 262 (0.76%) | 0 / 307 (0.00%) | 1 / 130 (0.77%) |
| occurrences (all)           | 3               | 0               | 1               |
| Escherichia infection       |                 |                 |                 |
| subjects affected / exposed | 2 / 262 (0.76%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)           | 2               | 0               | 0               |
| Herpes zoster               |                 |                 |                 |
| subjects affected / exposed | 2 / 262 (0.76%) | 2 / 307 (0.65%) | 1 / 130 (0.77%) |
| occurrences (all)           | 2               | 2               | 1               |
| Oral herpes                 |                 |                 |                 |
| subjects affected / exposed | 2 / 262 (0.76%) | 2 / 307 (0.65%) | 1 / 130 (0.77%) |
| occurrences (all)           | 3               | 2               | 1               |
| Oral infection              |                 |                 |                 |
| subjects affected / exposed | 2 / 262 (0.76%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)           | 2               | 0               | 0               |
| Pharyngitis                 |                 |                 |                 |
| subjects affected / exposed | 2 / 262 (0.76%) | 2 / 307 (0.65%) | 0 / 130 (0.00%) |
| occurrences (all)           | 2               | 2               | 0               |
| Skin infection              |                 |                 |                 |
| subjects affected / exposed | 2 / 262 (0.76%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)           | 2               | 1               | 0               |
| Acute sinusitis             |                 |                 |                 |
| subjects affected / exposed | 1 / 262 (0.38%) | 1 / 307 (0.33%) | 1 / 130 (0.77%) |
| occurrences (all)           | 1               | 2               | 1               |
| Asymptomatic bacteriuria    |                 |                 |                 |
| subjects affected / exposed | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)           | 1               | 0               | 0               |
| Bacteraemia                 |                 |                 |                 |
| subjects affected / exposed | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 1 / 130 (0.77%) |
| occurrences (all)           | 1               | 0               | 1               |

|                                           |                 |                 |                 |
|-------------------------------------------|-----------------|-----------------|-----------------|
| Bronchiolitis                             |                 |                 |                 |
| subjects affected / exposed               | 1 / 262 (0.38%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)                         | 1               | 1               | 0               |
| Cellulitis of male external genital organ |                 |                 |                 |
| subjects affected / exposed               | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)                         | 2               | 0               | 0               |
| Clostridium difficile colitis             |                 |                 |                 |
| subjects affected / exposed               | 1 / 262 (0.38%) | 3 / 307 (0.98%) | 3 / 130 (2.31%) |
| occurrences (all)                         | 1               | 3               | 4               |
| Clostridium difficile infection           |                 |                 |                 |
| subjects affected / exposed               | 1 / 262 (0.38%) | 1 / 307 (0.33%) | 1 / 130 (0.77%) |
| occurrences (all)                         | 1               | 1               | 1               |
| Cytomegalovirus viraemia                  |                 |                 |                 |
| subjects affected / exposed               | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)                         | 1               | 0               | 0               |
| Ear infection                             |                 |                 |                 |
| subjects affected / exposed               | 1 / 262 (0.38%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)                         | 1               | 1               | 0               |
| Enterocolitis infectious                  |                 |                 |                 |
| subjects affected / exposed               | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)                         | 2               | 0               | 0               |
| Epididymitis                              |                 |                 |                 |
| subjects affected / exposed               | 1 / 262 (0.38%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)                         | 1               | 1               | 0               |
| Fungal infection                          |                 |                 |                 |
| subjects affected / exposed               | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)                         | 1               | 0               | 0               |
| Gastric infection                         |                 |                 |                 |
| subjects affected / exposed               | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)                         | 1               | 0               | 0               |
| Hordeolum                                 |                 |                 |                 |
| subjects affected / exposed               | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)                         | 1               | 0               | 0               |
| Gastrointestinal infection                |                 |                 |                 |

|                                             |                 |                 |                 |
|---------------------------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed                 | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)                           | 1               | 0               | 0               |
| Infection                                   |                 |                 |                 |
| subjects affected / exposed                 | 1 / 262 (0.38%) | 2 / 307 (0.65%) | 0 / 130 (0.00%) |
| occurrences (all)                           | 2               | 3               | 0               |
| Latent tuberculosis                         |                 |                 |                 |
| subjects affected / exposed                 | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)                           | 1               | 0               | 0               |
| Molluscum contagiosum                       |                 |                 |                 |
| subjects affected / exposed                 | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)                           | 1               | 0               | 0               |
| Nail infection                              |                 |                 |                 |
| subjects affected / exposed                 | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)                           | 1               | 0               | 0               |
| Nasal herpes                                |                 |                 |                 |
| subjects affected / exposed                 | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)                           | 1               | 0               | 0               |
| Oesophageal candidiasis                     |                 |                 |                 |
| subjects affected / exposed                 | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 1 / 130 (0.77%) |
| occurrences (all)                           | 1               | 0               | 1               |
| Post procedural infection                   |                 |                 |                 |
| subjects affected / exposed                 | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)                           | 1               | 0               | 0               |
| Proctitis herpes                            |                 |                 |                 |
| subjects affected / exposed                 | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)                           | 1               | 0               | 0               |
| Pulpitis dental                             |                 |                 |                 |
| subjects affected / exposed                 | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)                           | 1               | 0               | 0               |
| Scrotal infection                           |                 |                 |                 |
| subjects affected / exposed <sup>[20]</sup> | 1 / 157 (0.64%) | 0 / 168 (0.00%) | 0 / 78 (0.00%)  |
| occurrences (all)                           | 1               | 0               | 0               |
| Sialoadenitis                               |                 |                 |                 |
| subjects affected / exposed                 | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)                           | 2               | 0               | 0               |
| Tinea cruris                                |                 |                 |                 |

|                                             |                 |                 |                 |
|---------------------------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed                 | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)                           | 1               | 0               | 0               |
| Tooth infection                             |                 |                 |                 |
| subjects affected / exposed                 | 1 / 262 (0.38%) | 3 / 307 (0.98%) | 0 / 130 (0.00%) |
| occurrences (all)                           | 1               | 4               | 0               |
| Vaginal infection                           |                 |                 |                 |
| subjects affected / exposed <sup>[21]</sup> | 1 / 105 (0.95%) | 1 / 139 (0.72%) | 0 / 52 (0.00%)  |
| occurrences (all)                           | 1               | 1               | 0               |
| Viral infection                             |                 |                 |                 |
| subjects affected / exposed                 | 1 / 262 (0.38%) | 3 / 307 (0.98%) | 0 / 130 (0.00%) |
| occurrences (all)                           | 1               | 3               | 0               |
| Alpha haemolytic streptococcal infection    |                 |                 |                 |
| subjects affected / exposed                 | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)                           | 0               | 1               | 0               |
| COVID-19 pneumonia                          |                 |                 |                 |
| subjects affected / exposed                 | 0 / 262 (0.00%) | 2 / 307 (0.65%) | 0 / 130 (0.00%) |
| occurrences (all)                           | 0               | 3               | 0               |
| Campylobacter infection                     |                 |                 |                 |
| subjects affected / exposed                 | 0 / 262 (0.00%) | 0 / 307 (0.00%) | 1 / 130 (0.77%) |
| occurrences (all)                           | 0               | 0               | 1               |
| Enterocolitis viral                         |                 |                 |                 |
| subjects affected / exposed                 | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)                           | 0               | 1               | 0               |
| Erysipelas                                  |                 |                 |                 |
| subjects affected / exposed                 | 0 / 262 (0.00%) | 0 / 307 (0.00%) | 1 / 130 (0.77%) |
| occurrences (all)                           | 0               | 0               | 1               |
| Eye infection                               |                 |                 |                 |
| subjects affected / exposed                 | 0 / 262 (0.00%) | 2 / 307 (0.65%) | 0 / 130 (0.00%) |
| occurrences (all)                           | 0               | 2               | 0               |
| Fungal skin infection                       |                 |                 |                 |
| subjects affected / exposed                 | 0 / 262 (0.00%) | 2 / 307 (0.65%) | 2 / 130 (1.54%) |
| occurrences (all)                           | 0               | 2               | 2               |
| Gastroenteritis norovirus                   |                 |                 |                 |
| subjects affected / exposed                 | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)                           | 0               | 1               | 0               |

|                                  |                 |                 |                 |
|----------------------------------|-----------------|-----------------|-----------------|
| Gastroenteritis viral            |                 |                 |                 |
| subjects affected / exposed      | 0 / 262 (0.00%) | 2 / 307 (0.65%) | 1 / 130 (0.77%) |
| occurrences (all)                | 0               | 2               | 1               |
| Gastrointestinal viral infection |                 |                 |                 |
| subjects affected / exposed      | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)                | 0               | 1               | 0               |
| Gingivitis                       |                 |                 |                 |
| subjects affected / exposed      | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)                | 0               | 1               | 0               |
| Helicobacter gastritis           |                 |                 |                 |
| subjects affected / exposed      | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)                | 0               | 1               | 0               |
| Helicobacter infection           |                 |                 |                 |
| subjects affected / exposed      | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)                | 0               | 1               | 0               |
| Herpes simplex                   |                 |                 |                 |
| subjects affected / exposed      | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)                | 0               | 1               | 0               |
| Herpes virus infection           |                 |                 |                 |
| subjects affected / exposed      | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)                | 0               | 1               | 0               |
| Infected cyst                    |                 |                 |                 |
| subjects affected / exposed      | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)                | 0               | 1               | 0               |
| Kidney infection                 |                 |                 |                 |
| subjects affected / exposed      | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)                | 0               | 1               | 0               |
| Localised infection              |                 |                 |                 |
| subjects affected / exposed      | 0 / 262 (0.00%) | 0 / 307 (0.00%) | 1 / 130 (0.77%) |
| occurrences (all)                | 0               | 0               | 1               |
| Measles                          |                 |                 |                 |
| subjects affected / exposed      | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)                | 0               | 1               | 0               |
| Moraxella infection              |                 |                 |                 |
| subjects affected / exposed      | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)                | 0               | 1               | 0               |

|                             |                 |                 |                 |
|-----------------------------|-----------------|-----------------|-----------------|
| Neutropenic sepsis          |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)           | 0               | 1               | 0               |
| Onychomycosis               |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)           | 0               | 1               | 0               |
| Ophthalmic herpes simplex   |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)           | 0               | 1               | 0               |
| Oral fungal infection       |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 0 / 307 (0.00%) | 1 / 130 (0.77%) |
| occurrences (all)           | 0               | 0               | 1               |
| Periorbital cellulitis      |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)           | 0               | 1               | 0               |
| Pneumonia haemophilus       |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)           | 0               | 1               | 0               |
| Pulmonary mycosis           |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)           | 0               | 1               | 0               |
| Septic shock                |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)           | 0               | 1               | 0               |
| Skin bacterial infection    |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)           | 0               | 1               | 0               |
| Splenic infection           |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)           | 0               | 1               | 0               |
| Staphylococcal sepsis       |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)           | 0               | 1               | 0               |
| Streptococcal bacteraemia   |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 0 / 307 (0.00%) | 1 / 130 (0.77%) |
| occurrences (all)           | 0               | 0               | 1               |

|                                             |                   |                   |                   |
|---------------------------------------------|-------------------|-------------------|-------------------|
| Tinea pedis                                 |                   |                   |                   |
| subjects affected / exposed                 | 0 / 262 (0.00%)   | 1 / 307 (0.33%)   | 0 / 130 (0.00%)   |
| occurrences (all)                           | 0                 | 1                 | 0                 |
| Tinea versicolour                           |                   |                   |                   |
| subjects affected / exposed                 | 0 / 262 (0.00%)   | 1 / 307 (0.33%)   | 0 / 130 (0.00%)   |
| occurrences (all)                           | 0                 | 1                 | 0                 |
| Urinary tract infection enterococcal        |                   |                   |                   |
| subjects affected / exposed                 | 0 / 262 (0.00%)   | 1 / 307 (0.33%)   | 0 / 130 (0.00%)   |
| occurrences (all)                           | 0                 | 1                 | 0                 |
| Viral pharyngitis                           |                   |                   |                   |
| subjects affected / exposed                 | 0 / 262 (0.00%)   | 1 / 307 (0.33%)   | 0 / 130 (0.00%)   |
| occurrences (all)                           | 0                 | 1                 | 0                 |
| Viral upper respiratory tract infection     |                   |                   |                   |
| subjects affected / exposed                 | 0 / 262 (0.00%)   | 4 / 307 (1.30%)   | 1 / 130 (0.77%)   |
| occurrences (all)                           | 0                 | 4                 | 1                 |
| Vulvovaginal mycotic infection              |                   |                   |                   |
| subjects affected / exposed <sup>[22]</sup> | 0 / 105 (0.00%)   | 0 / 139 (0.00%)   | 1 / 52 (1.92%)    |
| occurrences (all)                           | 0                 | 0                 | 1                 |
| Wound infection                             |                   |                   |                   |
| subjects affected / exposed                 | 0 / 262 (0.00%)   | 2 / 307 (0.65%)   | 0 / 130 (0.00%)   |
| occurrences (all)                           | 0                 | 2                 | 0                 |
| Contusion                                   |                   |                   |                   |
| subjects affected / exposed                 | 10 / 262 (3.82%)  | 10 / 307 (3.26%)  | 5 / 130 (3.85%)   |
| occurrences (all)                           | 15                | 11                | 6                 |
| Ligament sprain                             |                   |                   |                   |
| subjects affected / exposed                 | 4 / 262 (1.53%)   | 2 / 307 (0.65%)   | 0 / 130 (0.00%)   |
| occurrences (all)                           | 4                 | 2                 | 0                 |
| Humerus fracture                            |                   |                   |                   |
| subjects affected / exposed                 | 2 / 262 (0.76%)   | 0 / 307 (0.00%)   | 0 / 130 (0.00%)   |
| occurrences (all)                           | 2                 | 0                 | 0                 |
| Metabolism and nutrition disorders          |                   |                   |                   |
| Hypokalaemia                                |                   |                   |                   |
| subjects affected / exposed                 | 38 / 262 (14.50%) | 37 / 307 (12.05%) | 25 / 130 (19.23%) |
| occurrences (all)                           | 57                | 62                | 38                |
| Decreased appetite                          |                   |                   |                   |

|                             |                   |                   |                   |
|-----------------------------|-------------------|-------------------|-------------------|
| subjects affected / exposed | 37 / 262 (14.12%) | 59 / 307 (19.22%) | 32 / 130 (24.62%) |
| occurrences (all)           | 45                | 83                | 35                |
| Hypomagnesaemia             |                   |                   |                   |
| subjects affected / exposed | 22 / 262 (8.40%)  | 20 / 307 (6.51%)  | 15 / 130 (11.54%) |
| occurrences (all)           | 31                | 26                | 22                |
| Dehydration                 |                   |                   |                   |
| subjects affected / exposed | 11 / 262 (4.20%)  | 18 / 307 (5.86%)  | 16 / 130 (12.31%) |
| occurrences (all)           | 13                | 20                | 20                |
| Hypophosphataemia           |                   |                   |                   |
| subjects affected / exposed | 11 / 262 (4.20%)  | 12 / 307 (3.91%)  | 6 / 130 (4.62%)   |
| occurrences (all)           | 13                | 22                | 15                |
| Hyponatraemia               |                   |                   |                   |
| subjects affected / exposed | 8 / 262 (3.05%)   | 6 / 307 (1.95%)   | 7 / 130 (5.38%)   |
| occurrences (all)           | 10                | 10                | 11                |
| Hypercalcaemia              |                   |                   |                   |
| subjects affected / exposed | 5 / 262 (1.91%)   | 7 / 307 (2.28%)   | 3 / 130 (2.31%)   |
| occurrences (all)           | 5                 | 10                | 3                 |
| Hyperglycaemia              |                   |                   |                   |
| subjects affected / exposed | 5 / 262 (1.91%)   | 8 / 307 (2.61%)   | 4 / 130 (3.08%)   |
| occurrences (all)           | 5                 | 10                | 6                 |
| Hyperuricaemia              |                   |                   |                   |
| subjects affected / exposed | 5 / 262 (1.91%)   | 11 / 307 (3.58%)  | 7 / 130 (5.38%)   |
| occurrences (all)           | 6                 | 14                | 7                 |
| Hypocalcaemia               |                   |                   |                   |
| subjects affected / exposed | 4 / 262 (1.53%)   | 11 / 307 (3.58%)  | 5 / 130 (3.85%)   |
| occurrences (all)           | 6                 | 18                | 5                 |
| Hypercholesterolaemia       |                   |                   |                   |
| subjects affected / exposed | 3 / 262 (1.15%)   | 4 / 307 (1.30%)   | 2 / 130 (1.54%)   |
| occurrences (all)           | 3                 | 8                 | 2                 |
| Hyperkalaemia               |                   |                   |                   |
| subjects affected / exposed | 3 / 262 (1.15%)   | 9 / 307 (2.93%)   | 0 / 130 (0.00%)   |
| occurrences (all)           | 3                 | 10                | 0                 |
| Tumour lysis syndrome       |                   |                   |                   |
| subjects affected / exposed | 3 / 262 (1.15%)   | 0 / 307 (0.00%)   | 0 / 130 (0.00%)   |
| occurrences (all)           | 3                 | 0                 | 0                 |
| Vitamin D deficiency        |                   |                   |                   |

|                             |                 |                 |                 |
|-----------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed | 3 / 262 (1.15%) | 5 / 307 (1.63%) | 0 / 130 (0.00%) |
| occurrences (all)           | 3               | 5               | 0               |
| Gout                        |                 |                 |                 |
| subjects affected / exposed | 2 / 262 (0.76%) | 5 / 307 (1.63%) | 1 / 130 (0.77%) |
| occurrences (all)           | 2               | 5               | 1               |
| Hyperlipidaemia             |                 |                 |                 |
| subjects affected / exposed | 2 / 262 (0.76%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)           | 2               | 0               | 0               |
| Hypertriglyceridaemia       |                 |                 |                 |
| subjects affected / exposed | 2 / 262 (0.76%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)           | 2               | 1               | 0               |
| Hypoalbuminaemia            |                 |                 |                 |
| subjects affected / exposed | 2 / 262 (0.76%) | 5 / 307 (1.63%) | 2 / 130 (1.54%) |
| occurrences (all)           | 2               | 5               | 4               |
| Hypoglycaemia               |                 |                 |                 |
| subjects affected / exposed | 2 / 262 (0.76%) | 5 / 307 (1.63%) | 0 / 130 (0.00%) |
| occurrences (all)           | 2               | 5               | 0               |
| Increased appetite          |                 |                 |                 |
| subjects affected / exposed | 2 / 262 (0.76%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)           | 2               | 1               | 0               |
| Acidosis                    |                 |                 |                 |
| subjects affected / exposed | 1 / 262 (0.38%) | 1 / 307 (0.33%) | 1 / 130 (0.77%) |
| occurrences (all)           | 1               | 1               | 1               |
| Diabetes mellitus           |                 |                 |                 |
| subjects affected / exposed | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 1 / 130 (0.77%) |
| occurrences (all)           | 1               | 0               | 1               |
| Fluid overload              |                 |                 |                 |
| subjects affected / exposed | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)           | 1               | 0               | 0               |
| Fluid retention             |                 |                 |                 |
| subjects affected / exposed | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 1 / 130 (0.77%) |
| occurrences (all)           | 1               | 0               | 1               |
| Iron deficiency             |                 |                 |                 |
| subjects affected / exposed | 1 / 262 (0.38%) | 1 / 307 (0.33%) | 1 / 130 (0.77%) |
| occurrences (all)           | 1               | 1               | 1               |
| Magnesium deficiency        |                 |                 |                 |

|                             |                 |                 |                 |
|-----------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)           | 1               | 0               | 0               |
| Malnutrition                |                 |                 |                 |
| subjects affected / exposed | 1 / 262 (0.38%) | 1 / 307 (0.33%) | 2 / 130 (1.54%) |
| occurrences (all)           | 1               | 1               | 2               |
| Metabolic acidosis          |                 |                 |                 |
| subjects affected / exposed | 1 / 262 (0.38%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)           | 1               | 1               | 0               |
| Type 2 diabetes mellitus    |                 |                 |                 |
| subjects affected / exposed | 1 / 262 (0.38%) | 0 / 307 (0.00%) | 0 / 130 (0.00%) |
| occurrences (all)           | 1               | 0               | 0               |
| Abnormal loss of weight     |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)           | 0               | 1               | 0               |
| Cachexia                    |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)           | 0               | 1               | 0               |
| Failure to thrive           |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)           | 0               | 1               | 0               |
| Hypermagnesaemia            |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 2 / 307 (0.65%) | 0 / 130 (0.00%) |
| occurrences (all)           | 0               | 2               | 0               |
| Hypernatraemia              |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)           | 0               | 1               | 0               |
| Hyperphosphataemia          |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 1 / 130 (0.77%) |
| occurrences (all)           | 0               | 1               | 1               |
| Hypochloraemia              |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 0 / 307 (0.00%) | 1 / 130 (0.77%) |
| occurrences (all)           | 0               | 0               | 1               |
| Hypoproteinaemia            |                 |                 |                 |
| subjects affected / exposed | 0 / 262 (0.00%) | 1 / 307 (0.33%) | 0 / 130 (0.00%) |
| occurrences (all)           | 0               | 1               | 0               |
| Obesity                     |                 |                 |                 |

|                             |                  |                  |                 |
|-----------------------------|------------------|------------------|-----------------|
| subjects affected / exposed | 0 / 262 (0.00%)  | 0 / 307 (0.00%)  | 1 / 130 (0.77%) |
| occurrences (all)           | 0                | 0                | 1               |
| Vitamin B12 deficiency      |                  |                  |                 |
| subjects affected / exposed | 0 / 262 (0.00%)  | 3 / 307 (0.98%)  | 0 / 130 (0.00%) |
| occurrences (all)           | 0                | 3                | 0               |
| Zinc deficiency             |                  |                  |                 |
| subjects affected / exposed | 0 / 262 (0.00%)  | 1 / 307 (0.33%)  | 0 / 130 (0.00%) |
| occurrences (all)           | 0                | 1                | 0               |
| Myalgia                     |                  |                  |                 |
| subjects affected / exposed | 14 / 262 (5.34%) | 24 / 307 (7.82%) | 4 / 130 (3.08%) |
| occurrences (all)           | 15               | 29               | 6               |
| Neck pain                   |                  |                  |                 |
| subjects affected / exposed | 12 / 262 (4.58%) | 5 / 307 (1.63%)  | 5 / 130 (3.85%) |
| occurrences (all)           | 13               | 5                | 5               |

| <b>Non-serious adverse events</b>                                      | Arm D: Ublituximab<br>Monotherapy | Arm E: Ublituximab<br>to Umbralisib (TGR-<br>1202) |  |
|------------------------------------------------------------------------|-----------------------------------|----------------------------------------------------|--|
| Total subjects affected by non-serious<br>adverse events               |                                   |                                                    |  |
| subjects affected / exposed                                            | 20 / 24 (83.33%)                  | 12 / 12 (100.00%)                                  |  |
| Neoplasms benign, malignant and<br>unspecified (incl cysts and polyps) |                                   |                                                    |  |
| Basal cell carcinoma                                                   |                                   |                                                    |  |
| subjects affected / exposed                                            | 1 / 24 (4.17%)                    | 0 / 12 (0.00%)                                     |  |
| occurrences (all)                                                      | 1                                 | 0                                                  |  |
| Lipoma                                                                 |                                   |                                                    |  |
| subjects affected / exposed                                            | 0 / 24 (0.00%)                    | 0 / 12 (0.00%)                                     |  |
| occurrences (all)                                                      | 0                                 | 0                                                  |  |
| Benign neoplasm of eye                                                 |                                   |                                                    |  |
| subjects affected / exposed                                            | 0 / 24 (0.00%)                    | 0 / 12 (0.00%)                                     |  |
| occurrences (all)                                                      | 0                                 | 0                                                  |  |
| Bowen's disease                                                        |                                   |                                                    |  |
| subjects affected / exposed                                            | 0 / 24 (0.00%)                    | 0 / 12 (0.00%)                                     |  |
| occurrences (all)                                                      | 0                                 | 0                                                  |  |
| Central nervous system lymphoma                                        |                                   |                                                    |  |
| subjects affected / exposed                                            | 0 / 24 (0.00%)                    | 0 / 12 (0.00%)                                     |  |
| occurrences (all)                                                      | 0                                 | 0                                                  |  |
| Haemangioma of skin                                                    |                                   |                                                    |  |

|                                          |                |                |  |
|------------------------------------------|----------------|----------------|--|
| subjects affected / exposed              | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)                        | 0              | 0              |  |
| Meningioma                               |                |                |  |
| subjects affected / exposed              | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)                        | 0              | 0              |  |
| Neoplasm skin                            |                |                |  |
| subjects affected / exposed              | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)                        | 0              | 0              |  |
| Seborrhoeic keratosis                    |                |                |  |
| subjects affected / exposed              | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)                        | 0              | 0              |  |
| Skin cancer                              |                |                |  |
| subjects affected / exposed              | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)                        | 0              | 0              |  |
| Squamous cell carcinoma of head and neck |                |                |  |
| subjects affected / exposed              | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)                        | 0              | 0              |  |
| Tumour pain                              |                |                |  |
| subjects affected / exposed              | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)                        | 0              | 0              |  |
| Cancer pain                              |                |                |  |
| subjects affected / exposed              | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)                        | 0              | 0              |  |
| Gastrointestinal tract adenoma           |                |                |  |
| subjects affected / exposed              | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)                        | 0              | 0              |  |
| Haemangioma                              |                |                |  |
| subjects affected / exposed              | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)                        | 0              | 0              |  |
| Neoplasm                                 |                |                |  |
| subjects affected / exposed              | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)                        | 0              | 0              |  |
| Oral neoplasm                            |                |                |  |
| subjects affected / exposed              | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)                        | 0              | 0              |  |

|                                                                                     |                      |                     |  |
|-------------------------------------------------------------------------------------|----------------------|---------------------|--|
| Skin neoplasm bleeding<br>subjects affected / exposed<br>occurrences (all)          | 0 / 24 (0.00%)<br>0  | 1 / 12 (8.33%)<br>1 |  |
| Squamous cell carcinoma<br>subjects affected / exposed<br>occurrences (all)         | 1 / 24 (4.17%)<br>1  | 0 / 12 (0.00%)<br>0 |  |
| Squamous cell carcinoma of skin<br>subjects affected / exposed<br>occurrences (all) | 0 / 24 (0.00%)<br>0  | 0 / 12 (0.00%)<br>0 |  |
| Vascular disorders                                                                  |                      |                     |  |
| Hypertension<br>subjects affected / exposed<br>occurrences (all)                    | 3 / 24 (12.50%)<br>5 | 0 / 12 (0.00%)<br>0 |  |
| Flushing<br>subjects affected / exposed<br>occurrences (all)                        | 3 / 24 (12.50%)<br>3 | 0 / 12 (0.00%)<br>0 |  |
| Hypotension<br>subjects affected / exposed<br>occurrences (all)                     | 0 / 24 (0.00%)<br>0  | 0 / 12 (0.00%)<br>0 |  |
| Hot flush<br>subjects affected / exposed<br>occurrences (all)                       | 0 / 24 (0.00%)<br>0  | 0 / 12 (0.00%)<br>0 |  |
| Deep vein thrombosis<br>subjects affected / exposed<br>occurrences (all)            | 0 / 24 (0.00%)<br>0  | 0 / 12 (0.00%)<br>0 |  |
| Haematoma<br>subjects affected / exposed<br>occurrences (all)                       | 0 / 24 (0.00%)<br>0  | 1 / 12 (8.33%)<br>1 |  |
| Lymphoedema<br>subjects affected / exposed<br>occurrences (all)                     | 0 / 24 (0.00%)<br>0  | 0 / 12 (0.00%)<br>0 |  |
| Thrombophlebitis superficial<br>subjects affected / exposed<br>occurrences (all)    | 0 / 24 (0.00%)<br>0  | 0 / 12 (0.00%)<br>0 |  |
| Arterial thrombosis                                                                 |                      |                     |  |

|                                 |                |                |  |
|---------------------------------|----------------|----------------|--|
| subjects affected / exposed     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)               | 0              | 0              |  |
| Embolism                        |                |                |  |
| subjects affected / exposed     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)               | 0              | 0              |  |
| Embolism venous                 |                |                |  |
| subjects affected / exposed     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)               | 0              | 0              |  |
| Haemorrhage                     |                |                |  |
| subjects affected / exposed     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)               | 0              | 0              |  |
| Hyperaemia                      |                |                |  |
| subjects affected / exposed     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)               | 0              | 0              |  |
| Pallor                          |                |                |  |
| subjects affected / exposed     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)               | 0              | 0              |  |
| Peripheral coldness             |                |                |  |
| subjects affected / exposed     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)               | 0              | 0              |  |
| Peripheral venous disease       |                |                |  |
| subjects affected / exposed     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)               | 0              | 0              |  |
| Subgaleal haematoma             |                |                |  |
| subjects affected / exposed     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)               | 0              | 0              |  |
| Varicose vein                   |                |                |  |
| subjects affected / exposed     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)               | 0              | 0              |  |
| Vascular insufficiency          |                |                |  |
| subjects affected / exposed     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)               | 0              | 0              |  |
| Vasculitis                      |                |                |  |
| subjects affected / exposed     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)               | 0              | 0              |  |
| Surgical and medical procedures |                |                |  |

|                                                      |                 |                 |  |
|------------------------------------------------------|-----------------|-----------------|--|
| Skin neoplasm excision                               |                 |                 |  |
| subjects affected / exposed                          | 0 / 24 (0.00%)  | 0 / 12 (0.00%)  |  |
| occurrences (all)                                    | 0               | 0               |  |
| Hip arthroplasty                                     |                 |                 |  |
| subjects affected / exposed                          | 0 / 24 (0.00%)  | 0 / 12 (0.00%)  |  |
| occurrences (all)                                    | 0               | 0               |  |
| Tooth extraction                                     |                 |                 |  |
| subjects affected / exposed                          | 0 / 24 (0.00%)  | 0 / 12 (0.00%)  |  |
| occurrences (all)                                    | 0               | 0               |  |
| Cancer surgery                                       |                 |                 |  |
| subjects affected / exposed                          | 0 / 24 (0.00%)  | 0 / 12 (0.00%)  |  |
| occurrences (all)                                    | 0               | 0               |  |
| Cataract operation                                   |                 |                 |  |
| subjects affected / exposed                          | 0 / 24 (0.00%)  | 0 / 12 (0.00%)  |  |
| occurrences (all)                                    | 0               | 0               |  |
| Cerumen removal                                      |                 |                 |  |
| subjects affected / exposed                          | 0 / 24 (0.00%)  | 0 / 12 (0.00%)  |  |
| occurrences (all)                                    | 0               | 0               |  |
| Knee arthroplasty                                    |                 |                 |  |
| subjects affected / exposed                          | 0 / 24 (0.00%)  | 0 / 12 (0.00%)  |  |
| occurrences (all)                                    | 0               | 0               |  |
| General disorders and administration site conditions |                 |                 |  |
| Fatigue                                              |                 |                 |  |
| subjects affected / exposed                          | 5 / 24 (20.83%) | 3 / 12 (25.00%) |  |
| occurrences (all)                                    | 5               | 3               |  |
| Oedema peripheral                                    |                 |                 |  |
| subjects affected / exposed                          | 4 / 24 (16.67%) | 2 / 12 (16.67%) |  |
| occurrences (all)                                    | 5               | 2               |  |
| Pyrexia                                              |                 |                 |  |
| subjects affected / exposed                          | 3 / 24 (12.50%) | 2 / 12 (16.67%) |  |
| occurrences (all)                                    | 3               | 2               |  |
| Asthenia                                             |                 |                 |  |
| subjects affected / exposed                          | 0 / 24 (0.00%)  | 0 / 12 (0.00%)  |  |
| occurrences (all)                                    | 0               | 0               |  |
| Chills                                               |                 |                 |  |

|                             |                |                |
|-----------------------------|----------------|----------------|
| subjects affected / exposed | 2 / 24 (8.33%) | 0 / 12 (0.00%) |
| occurrences (all)           | 3              | 0              |
| Non-cardiac chest pain      |                |                |
| subjects affected / exposed | 2 / 24 (8.33%) | 0 / 12 (0.00%) |
| occurrences (all)           | 2              | 0              |
| Pain                        |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Chest discomfort            |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Peripheral swelling         |                |                |
| subjects affected / exposed | 1 / 24 (4.17%) | 0 / 12 (0.00%) |
| occurrences (all)           | 1              | 0              |
| Feeling abnormal            |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Influenza like illness      |                |                |
| subjects affected / exposed | 1 / 24 (4.17%) | 0 / 12 (0.00%) |
| occurrences (all)           | 1              | 0              |
| Swelling                    |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Catheter site pain          |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Chest pain                  |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Face oedema                 |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Feeling hot                 |                |                |
| subjects affected / exposed | 1 / 24 (4.17%) | 0 / 12 (0.00%) |
| occurrences (all)           | 1              | 0              |
| Gait disturbance            |                |                |

|                                   |                |                |
|-----------------------------------|----------------|----------------|
| subjects affected / exposed       | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                 | 0              | 0              |
| Localised oedema                  |                |                |
| subjects affected / exposed       | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                 | 0              | 0              |
| Malaise                           |                |                |
| subjects affected / exposed       | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                 | 0              | 0              |
| Swelling face                     |                |                |
| subjects affected / exposed       | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                 | 0              | 0              |
| Administration site extravasation |                |                |
| subjects affected / exposed       | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                 | 0              | 0              |
| Adverse drug reaction             |                |                |
| subjects affected / exposed       | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                 | 0              | 0              |
| Axillary pain                     |                |                |
| subjects affected / exposed       | 1 / 24 (4.17%) | 0 / 12 (0.00%) |
| occurrences (all)                 | 1              | 0              |
| Catheter site swelling            |                |                |
| subjects affected / exposed       | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                 | 0              | 0              |
| Discomfort                        |                |                |
| subjects affected / exposed       | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                 | 0              | 0              |
| Early satiety                     |                |                |
| subjects affected / exposed       | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                 | 0              | 0              |
| Facial pain                       |                |                |
| subjects affected / exposed       | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                 | 0              | 0              |
| Feeling jittery                   |                |                |
| subjects affected / exposed       | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                 | 0              | 0              |
| Illness                           |                |                |

|                                       |                |                |
|---------------------------------------|----------------|----------------|
| subjects affected / exposed           | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                     | 0              | 0              |
| Injection site bruising               |                |                |
| subjects affected / exposed           | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                     | 0              | 0              |
| Mucosal inflammation                  |                |                |
| subjects affected / exposed           | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                     | 0              | 0              |
| Oedema                                |                |                |
| subjects affected / exposed           | 1 / 24 (4.17%) | 0 / 12 (0.00%) |
| occurrences (all)                     | 1              | 0              |
| Performance status decreased          |                |                |
| subjects affected / exposed           | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                     | 0              | 0              |
| Disease progression                   |                |                |
| subjects affected / exposed           | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                     | 0              | 0              |
| Drug intolerance                      |                |                |
| subjects affected / exposed           | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                     | 0              | 0              |
| Exercise tolerance decreased          |                |                |
| subjects affected / exposed           | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                     | 0              | 0              |
| Feeling cold                          |                |                |
| subjects affected / exposed           | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                     | 0              | 0              |
| General physical health deterioration |                |                |
| subjects affected / exposed           | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                     | 0              | 0              |
| Generalised oedema                    |                |                |
| subjects affected / exposed           | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                     | 0              | 0              |
| Mass                                  |                |                |
| subjects affected / exposed           | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                     | 0              | 0              |
| Mucosal hyperaemia                    |                |                |

|                             |                |                |  |
|-----------------------------|----------------|----------------|--|
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Nodule                      |                |                |  |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Sensation of foreign body   |                |                |  |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Temperature intolerance     |                |                |  |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Tenderness                  |                |                |  |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Thirst                      |                |                |  |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Tissue infiltration         |                |                |  |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Immune system disorders     |                |                |  |
| Hypersensitivity            |                |                |  |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Seasonal allergy            |                |                |  |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Drug hypersensitivity       |                |                |  |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Hypogammaglobulinaemia      |                |                |  |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Allergy to animal           |                |                |  |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |

|                                                                                                 |                     |                     |  |
|-------------------------------------------------------------------------------------------------|---------------------|---------------------|--|
| Contrast media allergy<br>subjects affected / exposed<br>occurrences (all)                      | 0 / 24 (0.00%)<br>0 | 0 / 12 (0.00%)<br>0 |  |
| Contrast media reaction<br>subjects affected / exposed<br>occurrences (all)                     | 0 / 24 (0.00%)<br>0 | 0 / 12 (0.00%)<br>0 |  |
| Immunodeficiency<br>subjects affected / exposed<br>occurrences (all)                            | 0 / 24 (0.00%)<br>0 | 0 / 12 (0.00%)<br>0 |  |
| Sarcoidosis<br>subjects affected / exposed<br>occurrences (all)                                 | 0 / 24 (0.00%)<br>0 | 0 / 12 (0.00%)<br>0 |  |
| Reproductive system and breast disorders                                                        |                     |                     |  |
| Scrotal oedema<br>subjects affected / exposed <sup>[3]</sup><br>occurrences (all)               | 0 / 16 (0.00%)<br>0 | 0 / 8 (0.00%)<br>0  |  |
| Oedema genital<br>subjects affected / exposed<br>occurrences (all)                              | 0 / 24 (0.00%)<br>0 | 0 / 12 (0.00%)<br>0 |  |
| Pelvic pain<br>subjects affected / exposed<br>occurrences (all)                                 | 0 / 24 (0.00%)<br>0 | 0 / 12 (0.00%)<br>0 |  |
| Vulvovaginal pain<br>subjects affected / exposed <sup>[4]</sup><br>occurrences (all)            | 0 / 8 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0  |  |
| Benign prostatic hyperplasia<br>subjects affected / exposed <sup>[5]</sup><br>occurrences (all) | 0 / 16 (0.00%)<br>0 | 0 / 8 (0.00%)<br>0  |  |
| Breast discolouration<br>subjects affected / exposed <sup>[6]</sup><br>occurrences (all)        | 0 / 8 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0  |  |
| Breast mass<br>subjects affected / exposed <sup>[7]</sup><br>occurrences (all)                  | 0 / 8 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0  |  |
| Breast oedema                                                                                   |                     |                     |  |

|                                             |                |                |
|---------------------------------------------|----------------|----------------|
| subjects affected / exposed <sup>[8]</sup>  | 0 / 8 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                           | 0              | 0              |
| Breast pain                                 |                |                |
| subjects affected / exposed <sup>[9]</sup>  | 0 / 8 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                           | 0              | 0              |
| Breast swelling                             |                |                |
| subjects affected / exposed <sup>[10]</sup> | 0 / 8 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                           | 0              | 0              |
| Genital lesion                              |                |                |
| subjects affected / exposed                 | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                           | 0              | 0              |
| Genital rash                                |                |                |
| subjects affected / exposed                 | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                           | 0              | 0              |
| Gynaecomastia                               |                |                |
| subjects affected / exposed <sup>[11]</sup> | 0 / 8 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                           | 0              | 0              |
| Menstruation irregular                      |                |                |
| subjects affected / exposed <sup>[12]</sup> | 0 / 8 (0.00%)  | 1 / 4 (25.00%) |
| occurrences (all)                           | 0              | 1              |
| Orchitis noninfective                       |                |                |
| subjects affected / exposed <sup>[13]</sup> | 0 / 16 (0.00%) | 0 / 8 (0.00%)  |
| occurrences (all)                           | 0              | 0              |
| Peyronie's disease                          |                |                |
| subjects affected / exposed <sup>[14]</sup> | 0 / 16 (0.00%) | 0 / 8 (0.00%)  |
| occurrences (all)                           | 0              | 0              |
| Testicular oedema                           |                |                |
| subjects affected / exposed <sup>[15]</sup> | 0 / 16 (0.00%) | 0 / 8 (0.00%)  |
| occurrences (all)                           | 0              | 0              |
| Testicular pain                             |                |                |
| subjects affected / exposed <sup>[16]</sup> | 0 / 16 (0.00%) | 0 / 8 (0.00%)  |
| occurrences (all)                           | 0              | 0              |
| Vaginal haemorrhage                         |                |                |
| subjects affected / exposed <sup>[17]</sup> | 0 / 8 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                           | 0              | 0              |
| Vulvovaginal dryness                        |                |                |

|                                                 |                 |                 |  |
|-------------------------------------------------|-----------------|-----------------|--|
| subjects affected / exposed <sup>[18]</sup>     | 0 / 8 (0.00%)   | 0 / 4 (0.00%)   |  |
| occurrences (all)                               | 0               | 0               |  |
| Vulvovaginal pruritus                           |                 |                 |  |
| subjects affected / exposed <sup>[19]</sup>     | 0 / 8 (0.00%)   | 0 / 4 (0.00%)   |  |
| occurrences (all)                               | 0               | 0               |  |
| Respiratory, thoracic and mediastinal disorders |                 |                 |  |
| Dyspnoea                                        |                 |                 |  |
| subjects affected / exposed                     | 1 / 24 (4.17%)  | 0 / 12 (0.00%)  |  |
| occurrences (all)                               | 1               | 0               |  |
| Cough                                           |                 |                 |  |
| subjects affected / exposed                     | 5 / 24 (20.83%) | 2 / 12 (16.67%) |  |
| occurrences (all)                               | 8               | 2               |  |
| Oropharyngeal pain                              |                 |                 |  |
| subjects affected / exposed                     | 1 / 24 (4.17%)  | 0 / 12 (0.00%)  |  |
| occurrences (all)                               | 1               | 0               |  |
| Pleural effusion                                |                 |                 |  |
| subjects affected / exposed                     | 0 / 24 (0.00%)  | 0 / 12 (0.00%)  |  |
| occurrences (all)                               | 0               | 0               |  |
| Productive cough                                |                 |                 |  |
| subjects affected / exposed                     | 0 / 24 (0.00%)  | 0 / 12 (0.00%)  |  |
| occurrences (all)                               | 0               | 0               |  |
| Dysphonia                                       |                 |                 |  |
| subjects affected / exposed                     | 0 / 24 (0.00%)  | 0 / 12 (0.00%)  |  |
| occurrences (all)                               | 0               | 0               |  |
| Nasal congestion                                |                 |                 |  |
| subjects affected / exposed                     | 1 / 24 (4.17%)  | 0 / 12 (0.00%)  |  |
| occurrences (all)                               | 2               | 0               |  |
| Chronic obstructive pulmonary disease           |                 |                 |  |
| subjects affected / exposed                     | 0 / 24 (0.00%)  | 0 / 12 (0.00%)  |  |
| occurrences (all)                               | 0               | 0               |  |
| Epistaxis                                       |                 |                 |  |
| subjects affected / exposed                     | 0 / 24 (0.00%)  | 0 / 12 (0.00%)  |  |
| occurrences (all)                               | 0               | 0               |  |
| Hypoxia                                         |                 |                 |  |

|                              |                |                |
|------------------------------|----------------|----------------|
| subjects affected / exposed  | 1 / 24 (4.17%) | 0 / 12 (0.00%) |
| occurrences (all)            | 1              | 0              |
| Pulmonary oedema             |                |                |
| subjects affected / exposed  | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)            | 0              | 0              |
| Respiratory tract congestion |                |                |
| subjects affected / exposed  | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)            | 0              | 0              |
| Rhinitis allergic            |                |                |
| subjects affected / exposed  | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)            | 0              | 0              |
| Upper-airway cough syndrome  |                |                |
| subjects affected / exposed  | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)            | 0              | 0              |
| Wheezing                     |                |                |
| subjects affected / exposed  | 1 / 24 (4.17%) | 0 / 12 (0.00%) |
| occurrences (all)            | 2              | 0              |
| Dyspnoea exertional          |                |                |
| subjects affected / exposed  | 1 / 24 (4.17%) | 0 / 12 (0.00%) |
| occurrences (all)            | 1              | 0              |
| Haemoptysis                  |                |                |
| subjects affected / exposed  | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)            | 0              | 0              |
| Hiccups                      |                |                |
| subjects affected / exposed  | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)            | 0              | 0              |
| Rhinorrhoea                  |                |                |
| subjects affected / exposed  | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)            | 0              | 0              |
| Throat irritation            |                |                |
| subjects affected / exposed  | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)            | 0              | 0              |
| Atelectasis                  |                |                |
| subjects affected / exposed  | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)            | 0              | 0              |
| Dry throat                   |                |                |

|                             |                |                |  |
|-----------------------------|----------------|----------------|--|
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Interstitial lung disease   |                |                |  |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Nasal obstruction           |                |                |  |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Nasal pruritus              |                |                |  |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Nasal ulcer                 |                |                |  |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Oropharyngeal swelling      |                |                |  |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Paranasal sinus discomfort  |                |                |  |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Pleurisy                    |                |                |  |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Pneumonitis                 |                |                |  |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Pulmonary embolism          |                |                |  |
| subjects affected / exposed | 1 / 24 (4.17%) | 0 / 12 (0.00%) |  |
| occurrences (all)           | 2              | 0              |  |
| Pulmonary hypertension      |                |                |  |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Pulmonary mass              |                |                |  |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Rales                       |                |                |  |

|                             |                |                |  |
|-----------------------------|----------------|----------------|--|
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Sinus congestion            |                |                |  |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Sinus pain                  |                |                |  |
| subjects affected / exposed | 1 / 24 (4.17%) | 0 / 12 (0.00%) |  |
| occurrences (all)           | 1              | 0              |  |
| Sleep apnoea syndrome       |                |                |  |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Throat tightness            |                |                |  |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Acute respiratory failure   |                |                |  |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Aspiration                  |                |                |  |
| subjects affected / exposed | 1 / 24 (4.17%) | 0 / 12 (0.00%) |  |
| occurrences (all)           | 1              | 0              |  |
| Asthma                      |                |                |  |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Bronchial hyperreactivity   |                |                |  |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Bronchial obstruction       |                |                |  |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Catarrh                     |                |                |  |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Laryngeal inflammation      |                |                |  |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Mediastinal shift           |                |                |  |

|                                |                |                |
|--------------------------------|----------------|----------------|
| subjects affected / exposed    | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)              | 0              | 0              |
| Nasal dryness                  |                |                |
| subjects affected / exposed    | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)              | 0              | 0              |
| Nasal mucosal ulcer            |                |                |
| subjects affected / exposed    | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)              | 0              | 0              |
| Nasal oedema                   |                |                |
| subjects affected / exposed    | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)              | 0              | 0              |
| Nasal polyps                   |                |                |
| subjects affected / exposed    | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)              | 0              | 0              |
| Nasal septum disorder          |                |                |
| subjects affected / exposed    | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)              | 0              | 0              |
| Paranasal sinus hypersecretion |                |                |
| subjects affected / exposed    | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)              | 0              | 0              |
| Pharyngeal erythema            |                |                |
| subjects affected / exposed    | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)              | 0              | 0              |
| Pharyngeal hypertrophy         |                |                |
| subjects affected / exposed    | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)              | 0              | 0              |
| Pleuritic pain                 |                |                |
| subjects affected / exposed    | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)              | 0              | 0              |
| Pneumothorax                   |                |                |
| subjects affected / exposed    | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)              | 0              | 0              |
| Respiration abnormal           |                |                |
| subjects affected / exposed    | 0 / 24 (0.00%) | 1 / 12 (8.33%) |
| occurrences (all)              | 0              | 1              |
| Respiratory failure            |                |                |

|                                |                |                |  |
|--------------------------------|----------------|----------------|--|
| subjects affected / exposed    | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)              | 0              | 0              |  |
| Respiratory tract inflammation |                |                |  |
| subjects affected / exposed    | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)              | 0              | 0              |  |
| Rhinalgia                      |                |                |  |
| subjects affected / exposed    | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)              | 0              | 0              |  |
| Rhonchi                        |                |                |  |
| subjects affected / exposed    | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)              | 0              | 0              |  |
| Snoring                        |                |                |  |
| subjects affected / exposed    | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)              | 0              | 0              |  |
| Sputum increased               |                |                |  |
| subjects affected / exposed    | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)              | 0              | 0              |  |
| Vasomotor rhinitis             |                |                |  |
| subjects affected / exposed    | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)              | 0              | 0              |  |
| Psychiatric disorders          |                |                |  |
| Insomnia                       |                |                |  |
| subjects affected / exposed    | 1 / 24 (4.17%) | 0 / 12 (0.00%) |  |
| occurrences (all)              | 1              | 0              |  |
| Anxiety                        |                |                |  |
| subjects affected / exposed    | 1 / 24 (4.17%) | 0 / 12 (0.00%) |  |
| occurrences (all)              | 1              | 0              |  |
| Agitation                      |                |                |  |
| subjects affected / exposed    | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)              | 0              | 0              |  |
| Confusional state              |                |                |  |
| subjects affected / exposed    | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)              | 0              | 0              |  |
| Depression                     |                |                |  |
| subjects affected / exposed    | 0 / 24 (0.00%) | 1 / 12 (8.33%) |  |
| occurrences (all)              | 0              | 1              |  |

|                             |                |                |
|-----------------------------|----------------|----------------|
| Restlessness                |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Sleep disorder              |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Delirium                    |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Depressed mood              |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Euphoric mood               |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Irritability                |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Mood swings                 |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Nightmare                   |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Poor quality sleep          |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Abnormal dreams             |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Affect lability             |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Bruxism                     |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |

|                             |                |                |  |
|-----------------------------|----------------|----------------|--|
| Disorientation              |                |                |  |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Emotional disorder          |                |                |  |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Hallucination               |                |                |  |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Mania                       |                |                |  |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Mental status changes       |                |                |  |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Mood altered                |                |                |  |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Nervousness                 |                |                |  |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Panic attack                |                |                |  |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Self-induced vomiting       |                |                |  |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Product issues              |                |                |  |
| Device leakage              |                |                |  |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Device breakage             |                |                |  |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Device occlusion            |                |                |  |

|                             |                |                |  |
|-----------------------------|----------------|----------------|--|
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Thrombosis in device        |                |                |  |
| subjects affected / exposed | 0 / 24 (0.00%) | 1 / 12 (8.33%) |  |
| occurrences (all)           | 0              | 1              |  |
| Hepatobiliary disorders     |                |                |  |
| Cholecystitis acute         |                |                |  |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Hepatic necrosis            |                |                |  |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Hepatitis                   |                |                |  |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Hepatocellular injury       |                |                |  |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Bile duct obstruction       |                |                |  |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Cholecystitis               |                |                |  |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Gallbladder polyp           |                |                |  |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Hepatic cirrhosis           |                |                |  |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Hepatic steatosis           |                |                |  |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Hepatitis acute             |                |                |  |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |

|                                                                                           |                     |                      |  |
|-------------------------------------------------------------------------------------------|---------------------|----------------------|--|
| Hyperbilirubinaemia<br>subjects affected / exposed<br>occurrences (all)                   | 0 / 24 (0.00%)<br>0 | 0 / 12 (0.00%)<br>0  |  |
| Liver disorder<br>subjects affected / exposed<br>occurrences (all)                        | 0 / 24 (0.00%)<br>0 | 0 / 12 (0.00%)<br>0  |  |
| Investigations                                                                            |                     |                      |  |
| Aspartate aminotransferase increased<br>subjects affected / exposed<br>occurrences (all)  | 1 / 24 (4.17%)<br>1 | 1 / 12 (8.33%)<br>4  |  |
| Alanine aminotransferase increased<br>subjects affected / exposed<br>occurrences (all)    | 1 / 24 (4.17%)<br>1 | 1 / 12 (8.33%)<br>7  |  |
| Neutrophil count decreased<br>subjects affected / exposed<br>occurrences (all)            | 1 / 24 (4.17%)<br>2 | 2 / 12 (16.67%)<br>6 |  |
| Blood creatinine increased<br>subjects affected / exposed<br>occurrences (all)            | 0 / 24 (0.00%)<br>0 | 1 / 12 (8.33%)<br>1  |  |
| Blood lactate dehydrogenase increased<br>subjects affected / exposed<br>occurrences (all) | 0 / 24 (0.00%)<br>0 | 0 / 12 (0.00%)<br>0  |  |
| Blood alkaline phosphatase increased<br>subjects affected / exposed<br>occurrences (all)  | 0 / 24 (0.00%)<br>0 | 0 / 12 (0.00%)<br>0  |  |
| Weight decreased<br>subjects affected / exposed<br>occurrences (all)                      | 1 / 24 (4.17%)<br>1 | 0 / 12 (0.00%)<br>0  |  |
| Blood bilirubin increased<br>subjects affected / exposed<br>occurrences (all)             | 0 / 24 (0.00%)<br>0 | 0 / 12 (0.00%)<br>0  |  |
| Platelet count decreased<br>subjects affected / exposed<br>occurrences (all)              | 1 / 24 (4.17%)<br>1 | 0 / 12 (0.00%)<br>0  |  |
| White blood cell count decreased                                                          |                     |                      |  |

|                                     |                |                |
|-------------------------------------|----------------|----------------|
| subjects affected / exposed         | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                   | 0              | 0              |
| Weight increased                    |                |                |
| subjects affected / exposed         | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                   | 0              | 0              |
| Lymphocyte count decreased          |                |                |
| subjects affected / exposed         | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                   | 0              | 0              |
| Blood magnesium decreased           |                |                |
| subjects affected / exposed         | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                   | 0              | 0              |
| Blood pressure increased            |                |                |
| subjects affected / exposed         | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                   | 0              | 0              |
| C-reactive protein increased        |                |                |
| subjects affected / exposed         | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                   | 0              | 0              |
| Hepatic enzyme increased            |                |                |
| subjects affected / exposed         | 1 / 24 (4.17%) | 0 / 12 (0.00%) |
| occurrences (all)                   | 1              | 0              |
| Blood uric acid increased           |                |                |
| subjects affected / exposed         | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                   | 0              | 0              |
| Ejection fraction decreased         |                |                |
| subjects affected / exposed         | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                   | 0              | 0              |
| Gamma-glutamyltransferase increased |                |                |
| subjects affected / exposed         | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                   | 0              | 0              |
| Glomerular filtration rate          |                |                |
| subjects affected / exposed         | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                   | 0              | 0              |
| Ammonia increased                   |                |                |
| subjects affected / exposed         | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                   | 0              | 0              |

|                                                                                      |                     |                     |
|--------------------------------------------------------------------------------------|---------------------|---------------------|
| Blood albumin decreased<br>subjects affected / exposed<br>occurrences (all)          | 0 / 24 (0.00%)<br>0 | 0 / 12 (0.00%)<br>0 |
| Blood bicarbonate decreased<br>subjects affected / exposed<br>occurrences (all)      | 0 / 24 (0.00%)<br>0 | 0 / 12 (0.00%)<br>0 |
| Blood calcium increased<br>subjects affected / exposed<br>occurrences (all)          | 0 / 24 (0.00%)<br>0 | 0 / 12 (0.00%)<br>0 |
| Blood cholesterol increased<br>subjects affected / exposed<br>occurrences (all)      | 0 / 24 (0.00%)<br>0 | 0 / 12 (0.00%)<br>0 |
| Blood glucose increased<br>subjects affected / exposed<br>occurrences (all)          | 0 / 24 (0.00%)<br>0 | 0 / 12 (0.00%)<br>0 |
| Blood immunoglobulin G decreased<br>subjects affected / exposed<br>occurrences (all) | 0 / 24 (0.00%)<br>0 | 0 / 12 (0.00%)<br>0 |
| Blood urea increased<br>subjects affected / exposed<br>occurrences (all)             | 0 / 24 (0.00%)<br>0 | 0 / 12 (0.00%)<br>0 |
| Blood urine present<br>subjects affected / exposed<br>occurrences (all)              | 0 / 24 (0.00%)<br>0 | 0 / 12 (0.00%)<br>0 |
| Cardiac murmur<br>subjects affected / exposed<br>occurrences (all)                   | 0 / 24 (0.00%)<br>0 | 0 / 12 (0.00%)<br>0 |
| Clostridium test positive<br>subjects affected / exposed<br>occurrences (all)        | 0 / 24 (0.00%)<br>0 | 0 / 12 (0.00%)<br>0 |
| Coronavirus test positive<br>subjects affected / exposed<br>occurrences (all)        | 0 / 24 (0.00%)<br>0 | 0 / 12 (0.00%)<br>0 |
| Cytomegalovirus test positive<br>subjects affected / exposed<br>occurrences (all)    | 0 / 24 (0.00%)<br>0 | 0 / 12 (0.00%)<br>0 |

|                                             |                |                |
|---------------------------------------------|----------------|----------------|
| ECG signs of myocardial ischaemia           |                |                |
| subjects affected / exposed                 | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                           | 0              | 0              |
| Electrocardiogram QT prolonged              |                |                |
| subjects affected / exposed                 | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                           | 0              | 0              |
| Haemoglobin decreased                       |                |                |
| subjects affected / exposed                 | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                           | 0              | 0              |
| Hepatic enzyme abnormal                     |                |                |
| subjects affected / exposed                 | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                           | 0              | 0              |
| Immunoglobulins decreased                   |                |                |
| subjects affected / exposed                 | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                           | 0              | 0              |
| Liver function test increased               |                |                |
| subjects affected / exposed                 | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                           | 0              | 0              |
| Magnetic resonance imaging brain abnormal   |                |                |
| subjects affected / exposed                 | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                           | 0              | 0              |
| Prostatic specific antigen increased        |                |                |
| subjects affected / exposed                 | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                           | 0              | 0              |
| Prothrombin time prolonged                  |                |                |
| subjects affected / exposed                 | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                           | 0              | 0              |
| Red blood cell sedimentation rate increased |                |                |
| subjects affected / exposed                 | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                           | 0              | 0              |
| Transaminases increased                     |                |                |
| subjects affected / exposed                 | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                           | 0              | 0              |
| Troponin increased                          |                |                |

|                                        |                |                |
|----------------------------------------|----------------|----------------|
| subjects affected / exposed            | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                      | 0              | 0              |
| Urinary sediment present               |                |                |
| subjects affected / exposed            | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                      | 0              | 0              |
| Vitamin B12 decreased                  |                |                |
| subjects affected / exposed            | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                      | 0              | 0              |
| Beta globulin decreased                |                |                |
| subjects affected / exposed            | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                      | 0              | 0              |
| Blood creatine phosphokinase increased |                |                |
| subjects affected / exposed            | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                      | 0              | 0              |
| Blood immunoglobulin A decreased       |                |                |
| subjects affected / exposed            | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                      | 0              | 0              |
| Blood immunoglobulin M increased       |                |                |
| subjects affected / exposed            | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                      | 0              | 0              |
| Blood iron decreased                   |                |                |
| subjects affected / exposed            | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                      | 0              | 0              |
| Blood potassium decreased              |                |                |
| subjects affected / exposed            | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                      | 0              | 0              |
| Blood prolactin increased              |                |                |
| subjects affected / exposed            | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                      | 0              | 0              |
| Blood testosterone decreased           |                |                |
| subjects affected / exposed            | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                      | 0              | 0              |
| Blood viscosity increased              |                |                |
| subjects affected / exposed            | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                      | 0              | 0              |

|                                                                                                                       |                     |                     |  |
|-----------------------------------------------------------------------------------------------------------------------|---------------------|---------------------|--|
| Body temperature decreased<br>subjects affected / exposed<br>occurrences (all)                                        | 0 / 24 (0.00%)<br>0 | 0 / 12 (0.00%)<br>0 |  |
| Body temperature increased<br>subjects affected / exposed<br>occurrences (all)                                        | 0 / 24 (0.00%)<br>0 | 0 / 12 (0.00%)<br>0 |  |
| Bone density decreased<br>subjects affected / exposed<br>occurrences (all)                                            | 0 / 24 (0.00%)<br>0 | 0 / 12 (0.00%)<br>0 |  |
| Breath sounds abnormal<br>subjects affected / exposed<br>occurrences (all)                                            | 0 / 24 (0.00%)<br>0 | 0 / 12 (0.00%)<br>0 |  |
| Eastern Cooperative Oncology Group<br>performance status worsened<br>subjects affected / exposed<br>occurrences (all) | 0 / 24 (0.00%)<br>0 | 0 / 12 (0.00%)<br>0 |  |
| Faecal calprotectin increased<br>subjects affected / exposed<br>occurrences (all)                                     | 0 / 24 (0.00%)<br>0 | 0 / 12 (0.00%)<br>0 |  |
| Haemoglobin increased<br>subjects affected / exposed<br>occurrences (all)                                             | 0 / 24 (0.00%)<br>0 | 0 / 12 (0.00%)<br>0 |  |
| Haemophilus test positive<br>subjects affected / exposed<br>occurrences (all)                                         | 0 / 24 (0.00%)<br>0 | 0 / 12 (0.00%)<br>0 |  |
| Heart rate increased<br>subjects affected / exposed<br>occurrences (all)                                              | 0 / 24 (0.00%)<br>0 | 0 / 12 (0.00%)<br>0 |  |
| Human rhinovirus positive<br>subjects affected / exposed<br>occurrences (all)                                         | 0 / 24 (0.00%)<br>0 | 0 / 12 (0.00%)<br>0 |  |
| Immature granulocyte count<br>increased<br>subjects affected / exposed<br>occurrences (all)                           | 0 / 24 (0.00%)<br>0 | 0 / 12 (0.00%)<br>0 |  |
| Immunoglobulins increased                                                                                             |                     |                     |  |

|                                          |                |                |  |
|------------------------------------------|----------------|----------------|--|
| subjects affected / exposed              | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)                        | 0              | 0              |  |
| International normalised ratio increased |                |                |  |
| subjects affected / exposed              | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)                        | 0              | 0              |  |
| Light chain analysis decreased           |                |                |  |
| subjects affected / exposed              | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)                        | 0              | 0              |  |
| Light chain analysis increased           |                |                |  |
| subjects affected / exposed              | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)                        | 0              | 0              |  |
| Lipase increased                         |                |                |  |
| subjects affected / exposed              | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)                        | 0              | 0              |  |
| Low density lipoprotein increased        |                |                |  |
| subjects affected / exposed              | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)                        | 0              | 0              |  |
| Lymphocyte count abnormal                |                |                |  |
| subjects affected / exposed              | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)                        | 0              | 0              |  |
| Lymphocyte count increased               |                |                |  |
| subjects affected / exposed              | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)                        | 0              | 0              |  |
| Monocyte count decreased                 |                |                |  |
| subjects affected / exposed              | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)                        | 0              | 0              |  |
| Neutrophil count increased               |                |                |  |
| subjects affected / exposed              | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)                        | 0              | 0              |  |
| Pedal pulse decreased                    |                |                |  |
| subjects affected / exposed              | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)                        | 0              | 0              |  |
| Platelet count increased                 |                |                |  |
| subjects affected / exposed              | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)                        | 0              | 0              |  |

|                                                |                 |                |  |
|------------------------------------------------|-----------------|----------------|--|
| Protein total decreased                        |                 |                |  |
| subjects affected / exposed                    | 0 / 24 (0.00%)  | 0 / 12 (0.00%) |  |
| occurrences (all)                              | 0               | 0              |  |
| Protein urine present                          |                 |                |  |
| subjects affected / exposed                    | 0 / 24 (0.00%)  | 0 / 12 (0.00%) |  |
| occurrences (all)                              | 0               | 0              |  |
| Red cell distribution width increased          |                 |                |  |
| subjects affected / exposed                    | 0 / 24 (0.00%)  | 0 / 12 (0.00%) |  |
| occurrences (all)                              | 0               | 0              |  |
| SARS-CoV-2 test positive                       |                 |                |  |
| subjects affected / exposed                    | 0 / 24 (0.00%)  | 1 / 12 (8.33%) |  |
| occurrences (all)                              | 0               | 1              |  |
| Serum ferritin decreased                       |                 |                |  |
| subjects affected / exposed                    | 0 / 24 (0.00%)  | 0 / 12 (0.00%) |  |
| occurrences (all)                              | 0               | 0              |  |
| Troponin I increased                           |                 |                |  |
| subjects affected / exposed                    | 0 / 24 (0.00%)  | 0 / 12 (0.00%) |  |
| occurrences (all)                              | 0               | 0              |  |
| Vitamin D decreased                            |                 |                |  |
| subjects affected / exposed                    | 0 / 24 (0.00%)  | 0 / 12 (0.00%) |  |
| occurrences (all)                              | 0               | 0              |  |
| White blood cell count increased               |                 |                |  |
| subjects affected / exposed                    | 0 / 24 (0.00%)  | 0 / 12 (0.00%) |  |
| occurrences (all)                              | 0               | 0              |  |
| Injury, poisoning and procedural complications |                 |                |  |
| Infusion related reaction                      |                 |                |  |
| subjects affected / exposed                    | 3 / 24 (12.50%) | 0 / 12 (0.00%) |  |
| occurrences (all)                              | 5               | 0              |  |
| Fall                                           |                 |                |  |
| subjects affected / exposed                    | 1 / 24 (4.17%)  | 1 / 12 (8.33%) |  |
| occurrences (all)                              | 1               | 1              |  |
| Skin laceration                                |                 |                |  |
| subjects affected / exposed                    | 0 / 24 (0.00%)  | 0 / 12 (0.00%) |  |
| occurrences (all)                              | 0               | 0              |  |
| Limb injury                                    |                 |                |  |

|                                  |                |                |
|----------------------------------|----------------|----------------|
| subjects affected / exposed      | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                | 0              | 0              |
| Procedural pain                  |                |                |
| subjects affected / exposed      | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                | 0              | 0              |
| Accidental overdose              |                |                |
| subjects affected / exposed      | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                | 0              | 0              |
| Arthropod bite                   |                |                |
| subjects affected / exposed      | 1 / 24 (4.17%) | 1 / 12 (8.33%) |
| occurrences (all)                | 1              | 1              |
| Arthropod sting                  |                |                |
| subjects affected / exposed      | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                | 0              | 0              |
| Lumbar vertebral fracture        |                |                |
| subjects affected / exposed      | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                | 0              | 0              |
| Radius fracture                  |                |                |
| subjects affected / exposed      | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                | 0              | 0              |
| Rib fracture                     |                |                |
| subjects affected / exposed      | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                | 0              | 0              |
| Skin abrasion                    |                |                |
| subjects affected / exposed      | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                | 0              | 0              |
| Thoracic vertebral fracture      |                |                |
| subjects affected / exposed      | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                | 0              | 0              |
| Traumatic intracranial haematoma |                |                |
| subjects affected / exposed      | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                | 0              | 0              |
| Wound secretion                  |                |                |
| subjects affected / exposed      | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                | 0              | 0              |
| Ankle fracture                   |                |                |

|                             |                |                |
|-----------------------------|----------------|----------------|
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Compression fracture        |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Concussion                  |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 1 / 12 (8.33%) |
| occurrences (all)           | 0              | 1              |
| Foreign body in ear         |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Hand fracture               |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Head injury                 |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Hip fracture                |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Joint injury                |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Lip injury                  |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Meniscus injury             |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Muscle strain               |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Overdose                    |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Periorbital haematoma       |                |                |

|                              |                |                |
|------------------------------|----------------|----------------|
| subjects affected / exposed  | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)            | 0              | 0              |
| Procedural hypotension       |                |                |
| subjects affected / exposed  | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)            | 0              | 0              |
| Product administration error |                |                |
| subjects affected / exposed  | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)            | 0              | 0              |
| Skin injury                  |                |                |
| subjects affected / exposed  | 1 / 24 (4.17%) | 0 / 12 (0.00%) |
| occurrences (all)            | 1              | 0              |
| Spinal compression fracture  |                |                |
| subjects affected / exposed  | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)            | 0              | 0              |
| Spinal fracture              |                |                |
| subjects affected / exposed  | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)            | 0              | 0              |
| Splenic injury               |                |                |
| subjects affected / exposed  | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)            | 0              | 0              |
| Stress fracture              |                |                |
| subjects affected / exposed  | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)            | 0              | 0              |
| Subdural haematoma           |                |                |
| subjects affected / exposed  | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)            | 0              | 0              |
| Tendon rupture               |                |                |
| subjects affected / exposed  | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)            | 0              | 0              |
| Thermal burn                 |                |                |
| subjects affected / exposed  | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)            | 0              | 0              |
| Tibia fracture               |                |                |
| subjects affected / exposed  | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)            | 0              | 0              |
| Wound complication           |                |                |

|                                                                                                            |                     |                     |  |
|------------------------------------------------------------------------------------------------------------|---------------------|---------------------|--|
| subjects affected / exposed<br>occurrences (all)                                                           | 0 / 24 (0.00%)<br>0 | 0 / 12 (0.00%)<br>0 |  |
| Congenital, familial and genetic disorders<br>Phimosis<br>subjects affected / exposed<br>occurrences (all) | 0 / 24 (0.00%)<br>0 | 0 / 12 (0.00%)<br>0 |  |
| Cardiac disorders<br>Tachycardia<br>subjects affected / exposed<br>occurrences (all)                       | 0 / 24 (0.00%)<br>0 | 0 / 12 (0.00%)<br>0 |  |
| Atrial fibrillation<br>subjects affected / exposed<br>occurrences (all)                                    | 0 / 24 (0.00%)<br>0 | 0 / 12 (0.00%)<br>0 |  |
| Palpitations<br>subjects affected / exposed<br>occurrences (all)                                           | 0 / 24 (0.00%)<br>0 | 0 / 12 (0.00%)<br>0 |  |
| Angina pectoris<br>subjects affected / exposed<br>occurrences (all)                                        | 0 / 24 (0.00%)<br>0 | 0 / 12 (0.00%)<br>0 |  |
| Cardiac failure<br>subjects affected / exposed<br>occurrences (all)                                        | 0 / 24 (0.00%)<br>0 | 0 / 12 (0.00%)<br>0 |  |
| Pericardial effusion<br>subjects affected / exposed<br>occurrences (all)                                   | 0 / 24 (0.00%)<br>0 | 0 / 12 (0.00%)<br>0 |  |
| Sinus tachycardia<br>subjects affected / exposed<br>occurrences (all)                                      | 0 / 24 (0.00%)<br>0 | 0 / 12 (0.00%)<br>0 |  |
| Atrial tachycardia<br>subjects affected / exposed<br>occurrences (all)                                     | 0 / 24 (0.00%)<br>0 | 0 / 12 (0.00%)<br>0 |  |
| Atrioventricular block complete<br>subjects affected / exposed<br>occurrences (all)                        | 0 / 24 (0.00%)<br>0 | 0 / 12 (0.00%)<br>0 |  |
| Atrioventricular block second degree                                                                       |                     |                     |  |

|                              |                |                |  |
|------------------------------|----------------|----------------|--|
| subjects affected / exposed  | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)            | 0              | 0              |  |
| Cardiac failure congestive   |                |                |  |
| subjects affected / exposed  | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)            | 0              | 0              |  |
| Cardiomyopathy               |                |                |  |
| subjects affected / exposed  | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)            | 0              | 0              |  |
| Coronary artery disease      |                |                |  |
| subjects affected / exposed  | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)            | 0              | 0              |  |
| Sinus bradycardia            |                |                |  |
| subjects affected / exposed  | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)            | 0              | 0              |  |
| Ventricular extrasystoles    |                |                |  |
| subjects affected / exposed  | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)            | 0              | 0              |  |
| Aortic valve incompetence    |                |                |  |
| subjects affected / exposed  | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)            | 0              | 0              |  |
| Arrhythmia                   |                |                |  |
| subjects affected / exposed  | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)            | 0              | 0              |  |
| Bradycardia                  |                |                |  |
| subjects affected / exposed  | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)            | 0              | 0              |  |
| Cardiovascular insufficiency |                |                |  |
| subjects affected / exposed  | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)            | 0              | 0              |  |
| Extrasystoles                |                |                |  |
| subjects affected / exposed  | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)            | 0              | 0              |  |
| Mitral valve incompetence    |                |                |  |
| subjects affected / exposed  | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)            | 0              | 0              |  |
| Pericarditis constrictive    |                |                |  |

|                               |                 |                 |  |
|-------------------------------|-----------------|-----------------|--|
| subjects affected / exposed   | 0 / 24 (0.00%)  | 0 / 12 (0.00%)  |  |
| occurrences (all)             | 0               | 0               |  |
| Supraventricular tachycardia  |                 |                 |  |
| subjects affected / exposed   | 0 / 24 (0.00%)  | 0 / 12 (0.00%)  |  |
| occurrences (all)             | 0               | 0               |  |
| Nervous system disorders      |                 |                 |  |
| Headache                      |                 |                 |  |
| subjects affected / exposed   | 2 / 24 (8.33%)  | 0 / 12 (0.00%)  |  |
| occurrences (all)             | 2               | 0               |  |
| Dizziness                     |                 |                 |  |
| subjects affected / exposed   | 4 / 24 (16.67%) | 3 / 12 (25.00%) |  |
| occurrences (all)             | 4               | 3               |  |
| Dysgeusia                     |                 |                 |  |
| subjects affected / exposed   | 1 / 24 (4.17%)  | 1 / 12 (8.33%)  |  |
| occurrences (all)             | 1               | 1               |  |
| Paraesthesia                  |                 |                 |  |
| subjects affected / exposed   | 0 / 24 (0.00%)  | 0 / 12 (0.00%)  |  |
| occurrences (all)             | 0               | 0               |  |
| Tremor                        |                 |                 |  |
| subjects affected / exposed   | 0 / 24 (0.00%)  | 1 / 12 (8.33%)  |  |
| occurrences (all)             | 0               | 1               |  |
| Neuropathy peripheral         |                 |                 |  |
| subjects affected / exposed   | 1 / 24 (4.17%)  | 0 / 12 (0.00%)  |  |
| occurrences (all)             | 1               | 0               |  |
| Somnolence                    |                 |                 |  |
| subjects affected / exposed   | 0 / 24 (0.00%)  | 0 / 12 (0.00%)  |  |
| occurrences (all)             | 0               | 0               |  |
| Memory impairment             |                 |                 |  |
| subjects affected / exposed   | 0 / 24 (0.00%)  | 0 / 12 (0.00%)  |  |
| occurrences (all)             | 0               | 0               |  |
| Peripheral sensory neuropathy |                 |                 |  |
| subjects affected / exposed   | 1 / 24 (4.17%)  | 0 / 12 (0.00%)  |  |
| occurrences (all)             | 1               | 0               |  |
| Syncope                       |                 |                 |  |
| subjects affected / exposed   | 0 / 24 (0.00%)  | 0 / 12 (0.00%)  |  |
| occurrences (all)             | 0               | 0               |  |

|                             |                |                |
|-----------------------------|----------------|----------------|
| Dysarthria                  |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Dyskinesia                  |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Hypoaesthesia               |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Lethargy                    |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Taste disorder              |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Amnesia                     |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Aphasia                     |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Balance disorder            |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Burning feet syndrome       |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Carotid artery dissection   |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Disturbance in attention    |                |                |
| subjects affected / exposed | 1 / 24 (4.17%) | 0 / 12 (0.00%) |
| occurrences (all)           | 1              | 0              |
| Dizziness postural          |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |

|                                 |                |                |
|---------------------------------|----------------|----------------|
| Extrapyramidal disorder         |                |                |
| subjects affected / exposed     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)               | 0              | 0              |
| Facial paralysis                |                |                |
| subjects affected / exposed     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)               | 0              | 0              |
| Loss of consciousness           |                |                |
| subjects affected / exposed     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)               | 0              | 0              |
| Muscle contractions involuntary |                |                |
| subjects affected / exposed     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)               | 0              | 0              |
| Neuralgia                       |                |                |
| subjects affected / exposed     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)               | 0              | 0              |
| Notalgia paraesthetica          |                |                |
| subjects affected / exposed     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)               | 0              | 0              |
| Presyncope                      |                |                |
| subjects affected / exposed     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)               | 0              | 0              |
| Restless legs syndrome          |                |                |
| subjects affected / exposed     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)               | 0              | 0              |
| Seizure                         |                |                |
| subjects affected / exposed     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)               | 0              | 0              |
| Ageusia                         |                |                |
| subjects affected / exposed     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)               | 0              | 0              |
| Anosmia                         |                |                |
| subjects affected / exposed     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)               | 0              | 0              |
| Burning sensation               |                |                |
| subjects affected / exposed     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)               | 0              | 0              |

|                                  |                |                |
|----------------------------------|----------------|----------------|
| Carpal tunnel syndrome           |                |                |
| subjects affected / exposed      | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                | 0              | 0              |
| Cervical radiculopathy           |                |                |
| subjects affected / exposed      | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                | 0              | 0              |
| Cognitive disorder               |                |                |
| subjects affected / exposed      | 0 / 24 (0.00%) | 1 / 12 (8.33%) |
| occurrences (all)                | 0              | 1              |
| Coordination abnormal            |                |                |
| subjects affected / exposed      | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                | 0              | 0              |
| Depressed level of consciousness |                |                |
| subjects affected / exposed      | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                | 0              | 0              |
| Encephalopathy                   |                |                |
| subjects affected / exposed      | 1 / 24 (4.17%) | 0 / 12 (0.00%) |
| occurrences (all)                | 1              | 0              |
| Haemorrhage intracranial         |                |                |
| subjects affected / exposed      | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                | 0              | 0              |
| Head discomfort                  |                |                |
| subjects affected / exposed      | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                | 0              | 0              |
| Hemiparesis                      |                |                |
| subjects affected / exposed      | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                | 0              | 0              |
| Hypogeusia                       |                |                |
| subjects affected / exposed      | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                | 0              | 0              |
| Intracranial aneurysm            |                |                |
| subjects affected / exposed      | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                | 0              | 0              |
| Lumbar radiculopathy             |                |                |
| subjects affected / exposed      | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                | 0              | 0              |

|                             |                |                |
|-----------------------------|----------------|----------------|
| Metabolic encephalopathy    |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Nerve compression           |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Parosmia                    |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Peripheral motor neuropathy |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Polyneuropathy              |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Post herpetic neuralgia     |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Psychomotor hyperactivity   |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Sciatica                    |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Sensory loss                |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Sinus headache              |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Spinal cord compression     |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Trigeminal neuralgia        |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |

|                                                                            |                      |                      |  |
|----------------------------------------------------------------------------|----------------------|----------------------|--|
| Vascular headache<br>subjects affected / exposed<br>occurrences (all)      | 0 / 24 (0.00%)<br>0  | 0 / 12 (0.00%)<br>0  |  |
| Blood and lymphatic system disorders                                       |                      |                      |  |
| Neutropenia<br>subjects affected / exposed<br>occurrences (all)            | 3 / 24 (12.50%)<br>4 | 3 / 12 (25.00%)<br>7 |  |
| Anaemia<br>subjects affected / exposed<br>occurrences (all)                | 1 / 24 (4.17%)<br>2  | 2 / 12 (16.67%)<br>6 |  |
| Thrombocytopenia<br>subjects affected / exposed<br>occurrences (all)       | 1 / 24 (4.17%)<br>1  | 4 / 12 (33.33%)<br>5 |  |
| Lymph node pain<br>subjects affected / exposed<br>occurrences (all)        | 1 / 24 (4.17%)<br>1  | 1 / 12 (8.33%)<br>1  |  |
| Lymphopenia<br>subjects affected / exposed<br>occurrences (all)            | 0 / 24 (0.00%)<br>0  | 0 / 12 (0.00%)<br>0  |  |
| Leukopenia<br>subjects affected / exposed<br>occurrences (all)             | 1 / 24 (4.17%)<br>1  | 0 / 12 (0.00%)<br>0  |  |
| Febrile neutropenia<br>subjects affected / exposed<br>occurrences (all)    | 0 / 24 (0.00%)<br>0  | 0 / 12 (0.00%)<br>0  |  |
| Lymphadenopathy<br>subjects affected / exposed<br>occurrences (all)        | 1 / 24 (4.17%)<br>1  | 0 / 12 (0.00%)<br>0  |  |
| Haemorrhagic diathesis<br>subjects affected / exposed<br>occurrences (all) | 0 / 24 (0.00%)<br>0  | 0 / 12 (0.00%)<br>0  |  |
| Normochromic anaemia<br>subjects affected / exposed<br>occurrences (all)   | 0 / 24 (0.00%)<br>0  | 0 / 12 (0.00%)<br>0  |  |
| Blood loss anaemia                                                         |                      |                      |  |

|                              |                |                |  |
|------------------------------|----------------|----------------|--|
| subjects affected / exposed  | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)            | 0              | 0              |  |
| Bone marrow failure          |                |                |  |
| subjects affected / exposed  | 0 / 24 (0.00%) | 1 / 12 (8.33%) |  |
| occurrences (all)            | 0              | 1              |  |
| Eosinophilia                 |                |                |  |
| subjects affected / exposed  | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)            | 0              | 0              |  |
| Iron deficiency anaemia      |                |                |  |
| subjects affected / exposed  | 0 / 24 (0.00%) | 1 / 12 (8.33%) |  |
| occurrences (all)            | 0              | 1              |  |
| Leukocytosis                 |                |                |  |
| subjects affected / exposed  | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)            | 0              | 0              |  |
| Lymphocytosis                |                |                |  |
| subjects affected / exposed  | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)            | 0              | 0              |  |
| Macrocytosis                 |                |                |  |
| subjects affected / exposed  | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)            | 0              | 0              |  |
| Microcytic anaemia           |                |                |  |
| subjects affected / exposed  | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)            | 0              | 0              |  |
| Pancytopenia                 |                |                |  |
| subjects affected / exposed  | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)            | 0              | 0              |  |
| Paratracheal lymphadenopathy |                |                |  |
| subjects affected / exposed  | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)            | 0              | 0              |  |
| Splenic infarction           |                |                |  |
| subjects affected / exposed  | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)            | 0              | 0              |  |
| Ear and labyrinth disorders  |                |                |  |
| Tinnitus                     |                |                |  |
| subjects affected / exposed  | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)            | 0              | 0              |  |

|                             |                |                |
|-----------------------------|----------------|----------------|
| Ear pain                    |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Vertigo                     |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Deafness                    |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Ear congestion              |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Ear pruritus                |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Ear swelling                |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| External ear inflammation   |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Hypoacusis                  |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Otorrhoea                   |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Vertigo positional          |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Deafness unilateral         |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Ear discomfort              |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |

|                              |                |                |  |
|------------------------------|----------------|----------------|--|
| Ear disorder                 |                |                |  |
| subjects affected / exposed  | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)            | 0              | 0              |  |
| Excessive cerumen production |                |                |  |
| subjects affected / exposed  | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)            | 0              | 0              |  |
| Presbycusis                  |                |                |  |
| subjects affected / exposed  | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)            | 0              | 0              |  |
| Eye disorders                |                |                |  |
| Vision blurred               |                |                |  |
| subjects affected / exposed  | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)            | 0              | 0              |  |
| Dry eye                      |                |                |  |
| subjects affected / exposed  | 0 / 24 (0.00%) | 1 / 12 (8.33%) |  |
| occurrences (all)            | 0              | 1              |  |
| Diplopia                     |                |                |  |
| subjects affected / exposed  | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)            | 0              | 0              |  |
| Lacrimation increased        |                |                |  |
| subjects affected / exposed  | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)            | 0              | 0              |  |
| Eyelid ptosis                |                |                |  |
| subjects affected / exposed  | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)            | 0              | 0              |  |
| Vitreous floaters            |                |                |  |
| subjects affected / exposed  | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)            | 0              | 0              |  |
| Cataract                     |                |                |  |
| subjects affected / exposed  | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)            | 0              | 0              |  |
| Conjunctival haemorrhage     |                |                |  |
| subjects affected / exposed  | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)            | 0              | 0              |  |
| Conjunctival hyperaemia      |                |                |  |

|                             |                |                |
|-----------------------------|----------------|----------------|
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Conjunctival oedema         |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Erythema of eyelid          |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Eye discharge               |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Eye disorder                |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Eye inflammation            |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Eye pain                    |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Eye pruritus                |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Eyelid oedema               |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Ocular discomfort           |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Periorbital oedema          |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Retinal haemorrhage         |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Visual acuity reduced       |                |                |

|                             |                |                |  |
|-----------------------------|----------------|----------------|--|
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Asthenopia                  |                |                |  |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Blepharitis                 |                |                |  |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Conjunctivitis allergic     |                |                |  |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Eye haemorrhage             |                |                |  |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Eye irritation              |                |                |  |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Eye swelling                |                |                |  |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Glaucoma                    |                |                |  |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Hypermetropia               |                |                |  |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Mydriasis                   |                |                |  |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Ocular hyperaemia           |                |                |  |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Photopsia                   |                |                |  |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Retinal detachment          |                |                |  |

|                                  |                 |                 |  |
|----------------------------------|-----------------|-----------------|--|
| subjects affected / exposed      | 0 / 24 (0.00%)  | 0 / 12 (0.00%)  |  |
| occurrences (all)                | 0               | 0               |  |
| Retinal tear                     |                 |                 |  |
| subjects affected / exposed      | 0 / 24 (0.00%)  | 0 / 12 (0.00%)  |  |
| occurrences (all)                | 0               | 0               |  |
| Scleral hyperaemia               |                 |                 |  |
| subjects affected / exposed      | 0 / 24 (0.00%)  | 0 / 12 (0.00%)  |  |
| occurrences (all)                | 0               | 0               |  |
| Visual impairment                |                 |                 |  |
| subjects affected / exposed      | 0 / 24 (0.00%)  | 0 / 12 (0.00%)  |  |
| occurrences (all)                | 0               | 0               |  |
| Xerophthalmia                    |                 |                 |  |
| subjects affected / exposed      | 0 / 24 (0.00%)  | 0 / 12 (0.00%)  |  |
| occurrences (all)                | 0               | 0               |  |
| Gastrointestinal disorders       |                 |                 |  |
| Diarrhoea                        |                 |                 |  |
| subjects affected / exposed      | 3 / 24 (12.50%) | 7 / 12 (58.33%) |  |
| occurrences (all)                | 5               | 16              |  |
| Nausea                           |                 |                 |  |
| subjects affected / exposed      | 2 / 24 (8.33%)  | 4 / 12 (33.33%) |  |
| occurrences (all)                | 3               | 4               |  |
| Vomiting                         |                 |                 |  |
| subjects affected / exposed      | 1 / 24 (4.17%)  | 3 / 12 (25.00%) |  |
| occurrences (all)                | 1               | 3               |  |
| Constipation                     |                 |                 |  |
| subjects affected / exposed      | 1 / 24 (4.17%)  | 1 / 12 (8.33%)  |  |
| occurrences (all)                | 1               | 1               |  |
| Abdominal pain                   |                 |                 |  |
| subjects affected / exposed      | 1 / 24 (4.17%)  | 0 / 12 (0.00%)  |  |
| occurrences (all)                | 1               | 0               |  |
| Gastrooesophageal reflux disease |                 |                 |  |
| subjects affected / exposed      | 0 / 24 (0.00%)  | 1 / 12 (8.33%)  |  |
| occurrences (all)                | 0               | 1               |  |
| Dyspepsia                        |                 |                 |  |
| subjects affected / exposed      | 2 / 24 (8.33%)  | 0 / 12 (0.00%)  |  |
| occurrences (all)                | 2               | 0               |  |

|                             |                |                |
|-----------------------------|----------------|----------------|
| Abdominal pain upper        |                |                |
| subjects affected / exposed | 1 / 24 (4.17%) | 0 / 12 (0.00%) |
| occurrences (all)           | 1              | 0              |
| Colitis                     |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Abdominal distension        |                |                |
| subjects affected / exposed | 1 / 24 (4.17%) | 0 / 12 (0.00%) |
| occurrences (all)           | 1              | 0              |
| Abdominal discomfort        |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Flatulence                  |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Dry mouth                   |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Dysphagia                   |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Stomatitis                  |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Anal incontinence           |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Haemorrhoids                |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 1 / 12 (8.33%) |
| occurrences (all)           | 0              | 1              |
| Inguinal hernia             |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Oral pain                   |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |

|                             |                |                |
|-----------------------------|----------------|----------------|
| Abdominal pain lower        |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Ascites                     |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Gastritis                   |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Toothache                   |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Eructation                  |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Haemorrhoidal haemorrhage   |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Mouth ulceration            |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Proctalgia                  |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Salivary hypersecretion     |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Abdominal hernia            |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Abdominal rigidity          |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Anal polyp                  |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |

|                                  |                |                |
|----------------------------------|----------------|----------------|
| Barrett's oesophagus             |                |                |
| subjects affected / exposed      | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                | 0              | 0              |
| Chapped lips                     |                |                |
| subjects affected / exposed      | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                | 0              | 0              |
| Diverticulum                     |                |                |
| subjects affected / exposed      | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                | 0              | 0              |
| Duodenitis                       |                |                |
| subjects affected / exposed      | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                | 0              | 0              |
| Enterocolitis                    |                |                |
| subjects affected / exposed      | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                | 0              | 0              |
| Epigastric discomfort            |                |                |
| subjects affected / exposed      | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                | 0              | 0              |
| Faeces discoloured               |                |                |
| subjects affected / exposed      | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                | 0              | 0              |
| Gastrointestinal pain            |                |                |
| subjects affected / exposed      | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                | 0              | 0              |
| Gastrointestinal sounds abnormal |                |                |
| subjects affected / exposed      | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                | 0              | 0              |
| Haematochezia                    |                |                |
| subjects affected / exposed      | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                | 0              | 0              |
| Hiatus hernia                    |                |                |
| subjects affected / exposed      | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                | 0              | 0              |
| Large intestine polyp            |                |                |
| subjects affected / exposed      | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                | 0              | 0              |

|                             |                |                |
|-----------------------------|----------------|----------------|
| Leukoplakia oral            |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Lip blister                 |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Mouth haemorrhage           |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Oesophagitis                |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Oral dysaesthesia           |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Oral mucosal eruption       |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Pancreatitis                |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Parotid gland enlargement   |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Proctitis                   |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Rectal haemorrhage          |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Salivary gland pain         |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Tongue coated               |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |

|                             |                |                |
|-----------------------------|----------------|----------------|
| Tongue disorder             |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Umbilical hernia            |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Abdominal adhesions         |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Abdominal mass              |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Abdominal tenderness        |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Abnormal faeces             |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Aphthous ulcer              |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Apical granuloma            |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Autoimmune enteropathy      |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Breath odour                |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Chronic gastritis           |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 1 / 12 (8.33%) |
| occurrences (all)           | 0              | 1              |
| Colitis microscopic         |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |

|                                           |                |                |  |
|-------------------------------------------|----------------|----------------|--|
| Defaecation urgency                       |                |                |  |
| subjects affected / exposed               | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)                         | 0              | 0              |  |
| Diverticulum intestinal                   |                |                |  |
| subjects affected / exposed               | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)                         | 0              | 0              |  |
| Faecal vomiting                           |                |                |  |
| subjects affected / exposed               | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)                         | 0              | 0              |  |
| Faeces soft                               |                |                |  |
| subjects affected / exposed               | 0 / 24 (0.00%) | 1 / 12 (8.33%) |  |
| occurrences (all)                         | 0              | 1              |  |
| Frequent bowel movements                  |                |                |  |
| subjects affected / exposed               | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)                         | 0              | 0              |  |
| Gastric disorder                          |                |                |  |
| subjects affected / exposed               | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)                         | 0              | 0              |  |
| Gastric mucosa erythema                   |                |                |  |
| subjects affected / exposed               | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)                         | 0              | 0              |  |
| Gastric ulcer                             |                |                |  |
| subjects affected / exposed               | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)                         | 0              | 0              |  |
| Gastritis haemorrhagic                    |                |                |  |
| subjects affected / exposed               | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)                         | 0              | 0              |  |
| Gastrooesophageal sphincter insufficiency |                |                |  |
| subjects affected / exposed               | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)                         | 0              | 0              |  |
| Gingival bleeding                         |                |                |  |
| subjects affected / exposed               | 0 / 24 (0.00%) | 1 / 12 (8.33%) |  |
| occurrences (all)                         | 0              | 1              |  |
| Gingival pain                             |                |                |  |

|                             |                |                |
|-----------------------------|----------------|----------------|
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Haematemesis                |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Hypoaesthesia oral          |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Ileus                       |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Impaired gastric emptying   |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 1 / 12 (8.33%) |
| occurrences (all)           | 0              | 1              |
| Intra-abdominal haematoma   |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Irritable bowel syndrome    |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Large intestinal ulcer      |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Lip exfoliation             |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Melaena                     |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Mesenteric vein thrombosis  |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Neutropenic colitis         |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Odynophagia                 |                |                |

|                             |                |                |  |
|-----------------------------|----------------|----------------|--|
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Oedematous pancreatitis     |                |                |  |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Oesophageal stenosis        |                |                |  |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Oral disorder               |                |                |  |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Oral mucosal blistering     |                |                |  |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Palatal disorder            |                |                |  |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Pancreatitis acute          |                |                |  |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Paraesthesia oral           |                |                |  |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Periodontal disease         |                |                |  |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Poor dental condition       |                |                |  |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Reflux gastritis            |                |                |  |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Stomatitis necrotising      |                |                |  |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Tongue ulceration           |                |                |  |

|                                        |                 |                 |  |
|----------------------------------------|-----------------|-----------------|--|
| subjects affected / exposed            | 0 / 24 (0.00%)  | 0 / 12 (0.00%)  |  |
| occurrences (all)                      | 0               | 0               |  |
| Varices oesophageal                    |                 |                 |  |
| subjects affected / exposed            | 0 / 24 (0.00%)  | 0 / 12 (0.00%)  |  |
| occurrences (all)                      | 0               | 0               |  |
| Skin and subcutaneous tissue disorders |                 |                 |  |
| Rash                                   |                 |                 |  |
| subjects affected / exposed            | 3 / 24 (12.50%) | 3 / 12 (25.00%) |  |
| occurrences (all)                      | 3               | 6               |  |
| Pruritus                               |                 |                 |  |
| subjects affected / exposed            | 1 / 24 (4.17%)  | 0 / 12 (0.00%)  |  |
| occurrences (all)                      | 1               | 0               |  |
| Erythema                               |                 |                 |  |
| subjects affected / exposed            | 0 / 24 (0.00%)  | 0 / 12 (0.00%)  |  |
| occurrences (all)                      | 0               | 0               |  |
| Alopecia                               |                 |                 |  |
| subjects affected / exposed            | 1 / 24 (4.17%)  | 0 / 12 (0.00%)  |  |
| occurrences (all)                      | 1               | 0               |  |
| Hyperhidrosis                          |                 |                 |  |
| subjects affected / exposed            | 0 / 24 (0.00%)  | 0 / 12 (0.00%)  |  |
| occurrences (all)                      | 0               | 0               |  |
| Night sweats                           |                 |                 |  |
| subjects affected / exposed            | 1 / 24 (4.17%)  | 0 / 12 (0.00%)  |  |
| occurrences (all)                      | 1               | 0               |  |
| Rash maculo-papular                    |                 |                 |  |
| subjects affected / exposed            | 1 / 24 (4.17%)  | 0 / 12 (0.00%)  |  |
| occurrences (all)                      | 1               | 0               |  |
| Dry skin                               |                 |                 |  |
| subjects affected / exposed            | 0 / 24 (0.00%)  | 0 / 12 (0.00%)  |  |
| occurrences (all)                      | 0               | 0               |  |
| Rash pruritic                          |                 |                 |  |
| subjects affected / exposed            | 0 / 24 (0.00%)  | 0 / 12 (0.00%)  |  |
| occurrences (all)                      | 0               | 0               |  |
| Skin mass                              |                 |                 |  |
| subjects affected / exposed            | 0 / 24 (0.00%)  | 0 / 12 (0.00%)  |  |
| occurrences (all)                      | 0               | 0               |  |

|                             |                |                |
|-----------------------------|----------------|----------------|
| Ecchymosis                  |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Skin ulcer                  |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Actinic keratosis           |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Dermatitis                  |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Pain of skin                |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Urticaria                   |                |                |
| subjects affected / exposed | 1 / 24 (4.17%) | 0 / 12 (0.00%) |
| occurrences (all)           | 1              | 0              |
| Angioedema                  |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Blister                     |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Decubitus ulcer             |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Dermatitis atopic           |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Eczema asteatotic           |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Exfoliative rash            |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |

|                             |                |                |
|-----------------------------|----------------|----------------|
| Hyperkeratosis              |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Hypersensitivity vasculitis |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Onychoclasia                |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Psoriasis                   |                |                |
| subjects affected / exposed | 1 / 24 (4.17%) | 0 / 12 (0.00%) |
| occurrences (all)           | 1              | 0              |
| Purpura                     |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Rash macular                |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Rosacea                     |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Skin burning sensation      |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Skin discolouration         |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Skin fissures               |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Skin irritation             |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Skin lesion                 |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |

|                                            |                |                |
|--------------------------------------------|----------------|----------------|
| Skin tightness                             |                |                |
| subjects affected / exposed                | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                          | 0              | 0              |
| Stasis dermatitis                          |                |                |
| subjects affected / exposed                | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                          | 0              | 0              |
| Cold sweat                                 |                |                |
| subjects affected / exposed                | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                          | 0              | 0              |
| Dermal cyst                                |                |                |
| subjects affected / exposed                | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                          | 0              | 0              |
| Dermatitis acneiform                       |                |                |
| subjects affected / exposed                | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                          | 0              | 0              |
| Dermatitis bullous                         |                |                |
| subjects affected / exposed                | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                          | 0              | 0              |
| Dermatitis exfoliative generalised         |                |                |
| subjects affected / exposed                | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                          | 0              | 0              |
| Drug eruption                              |                |                |
| subjects affected / exposed                | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                          | 0              | 0              |
| Eczema                                     |                |                |
| subjects affected / exposed                | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                          | 0              | 0              |
| Erythema multiforme                        |                |                |
| subjects affected / exposed                | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                          | 0              | 0              |
| Nail discolouration                        |                |                |
| subjects affected / exposed                | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                          | 0              | 0              |
| Palmar-plantar erythrodysesthesia syndrome |                |                |

|                             |                |                |
|-----------------------------|----------------|----------------|
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Papule                      |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Photosensitivity reaction   |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Purpura senile              |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Rash erythematous           |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Scab                        |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Scar pain                   |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Skin atrophy                |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Skin discomfort             |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Skin exfoliation            |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Skin hypopigmentation       |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Skin necrosis               |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Skin plaque                 |                |                |

|                             |                |                |  |
|-----------------------------|----------------|----------------|--|
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Skin reaction               |                |                |  |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Telangiectasia              |                |                |  |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Renal and urinary disorders |                |                |  |
| Pollakiuria                 |                |                |  |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Acute kidney injury         |                |                |  |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Haematuria                  |                |                |  |
| subjects affected / exposed | 0 / 24 (0.00%) | 1 / 12 (8.33%) |  |
| occurrences (all)           | 0              | 1              |  |
| Dysuria                     |                |                |  |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Chronic kidney disease      |                |                |  |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Proteinuria                 |                |                |  |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Calculus urinary            |                |                |  |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Micturition urgency         |                |                |  |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Polyuria                    |                |                |  |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |

|                             |                |                |
|-----------------------------|----------------|----------------|
| Renal failure               |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Strangury                   |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Ureteric stenosis           |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Urinary hesitation          |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Urinary retention           |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Urinary tract obstruction   |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Urine odour abnormal        |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Azotaemia                   |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Bladder discomfort          |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Haemorrhage urinary tract   |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Hydronephrosis              |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Hypertonic bladder          |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |

|                              |                |                |  |
|------------------------------|----------------|----------------|--|
| Nephrolithiasis              |                |                |  |
| subjects affected / exposed  | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)            | 0              | 0              |  |
| Nephropathy                  |                |                |  |
| subjects affected / exposed  | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)            | 0              | 0              |  |
| Nocturia                     |                |                |  |
| subjects affected / exposed  | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)            | 0              | 0              |  |
| Renal pain                   |                |                |  |
| subjects affected / exposed  | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)            | 0              | 0              |  |
| Ureterolithiasis             |                |                |  |
| subjects affected / exposed  | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)            | 0              | 0              |  |
| Urinary incontinence         |                |                |  |
| subjects affected / exposed  | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)            | 0              | 0              |  |
| Urinary tract pain           |                |                |  |
| subjects affected / exposed  | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)            | 0              | 0              |  |
| Endocrine disorders          |                |                |  |
| Hypothyroidism               |                |                |  |
| subjects affected / exposed  | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)            | 0              | 0              |  |
| Adrenal insufficiency        |                |                |  |
| subjects affected / exposed  | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)            | 0              | 0              |  |
| Hyperparathyroidism          |                |                |  |
| subjects affected / exposed  | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)            | 0              | 0              |  |
| Hypercalcaemia of malignancy |                |                |  |
| subjects affected / exposed  | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)            | 0              | 0              |  |
| Hyperthyroidism              |                |                |  |

|                                                 |                 |                |  |
|-------------------------------------------------|-----------------|----------------|--|
| subjects affected / exposed                     | 0 / 24 (0.00%)  | 0 / 12 (0.00%) |  |
| occurrences (all)                               | 0               | 0              |  |
| Musculoskeletal and connective tissue disorders |                 |                |  |
| Back pain                                       |                 |                |  |
| subjects affected / exposed                     | 4 / 24 (16.67%) | 1 / 12 (8.33%) |  |
| occurrences (all)                               | 6               | 1              |  |
| Arthralgia                                      |                 |                |  |
| subjects affected / exposed                     | 3 / 24 (12.50%) | 0 / 12 (0.00%) |  |
| occurrences (all)                               | 3               | 0              |  |
| Pain in extremity                               |                 |                |  |
| subjects affected / exposed                     | 3 / 24 (12.50%) | 1 / 12 (8.33%) |  |
| occurrences (all)                               | 4               | 1              |  |
| Muscle spasms                                   |                 |                |  |
| subjects affected / exposed                     | 1 / 24 (4.17%)  | 0 / 12 (0.00%) |  |
| occurrences (all)                               | 1               | 0              |  |
| Muscular weakness                               |                 |                |  |
| subjects affected / exposed                     | 1 / 24 (4.17%)  | 0 / 12 (0.00%) |  |
| occurrences (all)                               | 1               | 0              |  |
| Flank pain                                      |                 |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%)  | 0 / 12 (0.00%) |  |
| occurrences (all)                               | 0               | 0              |  |
| Groin pain                                      |                 |                |  |
| subjects affected / exposed                     | 2 / 24 (8.33%)  | 1 / 12 (8.33%) |  |
| occurrences (all)                               | 2               | 1              |  |
| Musculoskeletal pain                            |                 |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%)  | 0 / 12 (0.00%) |  |
| occurrences (all)                               | 0               | 0              |  |
| Joint swelling                                  |                 |                |  |
| subjects affected / exposed                     | 0 / 24 (0.00%)  | 0 / 12 (0.00%) |  |
| occurrences (all)                               | 0               | 0              |  |
| Bone pain                                       |                 |                |  |
| subjects affected / exposed                     | 1 / 24 (4.17%)  | 0 / 12 (0.00%) |  |
| occurrences (all)                               | 1               | 0              |  |
| Musculoskeletal discomfort                      |                 |                |  |

|                                |                |                |  |
|--------------------------------|----------------|----------------|--|
| subjects affected / exposed    | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)              | 0              | 0              |  |
| Arthritis                      |                |                |  |
| subjects affected / exposed    | 1 / 24 (4.17%) | 0 / 12 (0.00%) |  |
| occurrences (all)              | 1              | 0              |  |
| Muscle tightness               |                |                |  |
| subjects affected / exposed    | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)              | 0              | 0              |  |
| Musculoskeletal chest pain     |                |                |  |
| subjects affected / exposed    | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)              | 0              | 0              |  |
| Osteoporosis                   |                |                |  |
| subjects affected / exposed    | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)              | 0              | 0              |  |
| Pain in jaw                    |                |                |  |
| subjects affected / exposed    | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)              | 0              | 0              |  |
| Axillary mass                  |                |                |  |
| subjects affected / exposed    | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)              | 0              | 0              |  |
| Intervertebral disc protrusion |                |                |  |
| subjects affected / exposed    | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)              | 0              | 0              |  |
| Joint stiffness                |                |                |  |
| subjects affected / exposed    | 0 / 24 (0.00%) | 1 / 12 (8.33%) |  |
| occurrences (all)              | 0              | 1              |  |
| Osteoarthritis                 |                |                |  |
| subjects affected / exposed    | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)              | 0              | 0              |  |
| Periarthritis                  |                |                |  |
| subjects affected / exposed    | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)              | 0              | 0              |  |
| Psoriatic arthropathy          |                |                |  |
| subjects affected / exposed    | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)              | 0              | 0              |  |
| Rheumatoid arthritis           |                |                |  |

|                                 |                |                |
|---------------------------------|----------------|----------------|
| subjects affected / exposed     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)               | 0              | 0              |
| Rotator cuff syndrome           |                |                |
| subjects affected / exposed     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)               | 0              | 0              |
| Spinal osteoarthritis           |                |                |
| subjects affected / exposed     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)               | 0              | 0              |
| Spinal pain                     |                |                |
| subjects affected / exposed     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)               | 0              | 0              |
| Trigger finger                  |                |                |
| subjects affected / exposed     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)               | 0              | 0              |
| Bursitis                        |                |                |
| subjects affected / exposed     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)               | 0              | 0              |
| Coccydynia                      |                |                |
| subjects affected / exposed     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)               | 0              | 0              |
| Gouty arthritis                 |                |                |
| subjects affected / exposed     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)               | 0              | 0              |
| Joint range of motion decreased |                |                |
| subjects affected / exposed     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)               | 0              | 0              |
| Limb discomfort                 |                |                |
| subjects affected / exposed     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)               | 0              | 0              |
| Muscle fatigue                  |                |                |
| subjects affected / exposed     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)               | 0              | 0              |
| Muscle twitching                |                |                |
| subjects affected / exposed     | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)               | 0              | 0              |
| Musculoskeletal stiffness       |                |                |

|                                   |                 |                 |  |
|-----------------------------------|-----------------|-----------------|--|
| subjects affected / exposed       | 0 / 24 (0.00%)  | 0 / 12 (0.00%)  |  |
| occurrences (all)                 | 0               | 0               |  |
| Rhabdomyolysis                    |                 |                 |  |
| subjects affected / exposed       | 0 / 24 (0.00%)  | 0 / 12 (0.00%)  |  |
| occurrences (all)                 | 0               | 0               |  |
| Synovial cyst                     |                 |                 |  |
| subjects affected / exposed       | 0 / 24 (0.00%)  | 0 / 12 (0.00%)  |  |
| occurrences (all)                 | 0               | 0               |  |
| Tendon pain                       |                 |                 |  |
| subjects affected / exposed       | 0 / 24 (0.00%)  | 0 / 12 (0.00%)  |  |
| occurrences (all)                 | 0               | 0               |  |
| Tendonitis                        |                 |                 |  |
| subjects affected / exposed       | 0 / 24 (0.00%)  | 0 / 12 (0.00%)  |  |
| occurrences (all)                 | 0               | 0               |  |
| Infections and infestations       |                 |                 |  |
| Urinary tract infection           |                 |                 |  |
| subjects affected / exposed       | 1 / 24 (4.17%)  | 0 / 12 (0.00%)  |  |
| occurrences (all)                 | 1               | 0               |  |
| Pneumonia                         |                 |                 |  |
| subjects affected / exposed       | 0 / 24 (0.00%)  | 0 / 12 (0.00%)  |  |
| occurrences (all)                 | 0               | 0               |  |
| Upper respiratory tract infection |                 |                 |  |
| subjects affected / exposed       | 4 / 24 (16.67%) | 1 / 12 (8.33%)  |  |
| occurrences (all)                 | 4               | 1               |  |
| COVID-19                          |                 |                 |  |
| subjects affected / exposed       | 1 / 24 (4.17%)  | 0 / 12 (0.00%)  |  |
| occurrences (all)                 | 1               | 0               |  |
| Sinusitis                         |                 |                 |  |
| subjects affected / exposed       | 2 / 24 (8.33%)  | 2 / 12 (16.67%) |  |
| occurrences (all)                 | 2               | 3               |  |
| Oral candidiasis                  |                 |                 |  |
| subjects affected / exposed       | 0 / 24 (0.00%)  | 0 / 12 (0.00%)  |  |
| occurrences (all)                 | 0               | 0               |  |
| Bronchitis                        |                 |                 |  |
| subjects affected / exposed       | 1 / 24 (4.17%)  | 0 / 12 (0.00%)  |  |
| occurrences (all)                 | 1               | 0               |  |

|                                        |                |                |  |
|----------------------------------------|----------------|----------------|--|
| Candida infection                      |                |                |  |
| subjects affected / exposed            | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)                      | 0              | 0              |  |
| Nasopharyngitis                        |                |                |  |
| subjects affected / exposed            | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)                      | 0              | 0              |  |
| Respiratory tract infection            |                |                |  |
| subjects affected / exposed            | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)                      | 0              | 0              |  |
| Cytomegalovirus infection reactivation |                |                |  |
| subjects affected / exposed            | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)                      | 0              | 0              |  |
| Cytomegalovirus infection              |                |                |  |
| subjects affected / exposed            | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)                      | 0              | 0              |  |
| Folliculitis                           |                |                |  |
| subjects affected / exposed            | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)                      | 0              | 0              |  |
| Gastroenteritis                        |                |                |  |
| subjects affected / exposed            | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)                      | 0              | 0              |  |
| Influenza                              |                |                |  |
| subjects affected / exposed            | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)                      | 0              | 0              |  |
| Lower respiratory tract infection      |                |                |  |
| subjects affected / exposed            | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)                      | 0              | 0              |  |
| Rhinitis                               |                |                |  |
| subjects affected / exposed            | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)                      | 0              | 0              |  |
| Sepsis                                 |                |                |  |
| subjects affected / exposed            | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)                      | 0              | 0              |  |
| Cellulitis                             |                |                |  |

|                             |                |                |
|-----------------------------|----------------|----------------|
| subjects affected / exposed | 0 / 24 (0.00%) | 1 / 12 (8.33%) |
| occurrences (all)           | 0              | 1              |
| Chronic sinusitis           |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Conjunctivitis              |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Cystitis                    |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Diverticulitis              |                |                |
| subjects affected / exposed | 1 / 24 (4.17%) | 0 / 12 (0.00%) |
| occurrences (all)           | 1              | 0              |
| Escherichia infection       |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Herpes zoster               |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Oral herpes                 |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Oral infection              |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Pharyngitis                 |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Skin infection              |                |                |
| subjects affected / exposed | 1 / 24 (4.17%) | 0 / 12 (0.00%) |
| occurrences (all)           | 1              | 0              |
| Acute sinusitis             |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Asymptomatic bacteriuria    |                |                |

|                                           |                |                |
|-------------------------------------------|----------------|----------------|
| subjects affected / exposed               | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                         | 0              | 0              |
| Bacteraemia                               |                |                |
| subjects affected / exposed               | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                         | 0              | 0              |
| Bronchiolitis                             |                |                |
| subjects affected / exposed               | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                         | 0              | 0              |
| Cellulitis of male external genital organ |                |                |
| subjects affected / exposed               | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                         | 0              | 0              |
| Clostridium difficile colitis             |                |                |
| subjects affected / exposed               | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                         | 0              | 0              |
| Clostridium difficile infection           |                |                |
| subjects affected / exposed               | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                         | 0              | 0              |
| Cytomegalovirus viraemia                  |                |                |
| subjects affected / exposed               | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                         | 0              | 0              |
| Ear infection                             |                |                |
| subjects affected / exposed               | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                         | 0              | 0              |
| Enterocolitis infectious                  |                |                |
| subjects affected / exposed               | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                         | 0              | 0              |
| Epididymitis                              |                |                |
| subjects affected / exposed               | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                         | 0              | 0              |
| Fungal infection                          |                |                |
| subjects affected / exposed               | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                         | 0              | 0              |
| Gastric infection                         |                |                |
| subjects affected / exposed               | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                         | 0              | 0              |

|                                             |                |                |
|---------------------------------------------|----------------|----------------|
| Hordeolum                                   |                |                |
| subjects affected / exposed                 | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                           | 0              | 0              |
| Gastrointestinal infection                  |                |                |
| subjects affected / exposed                 | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                           | 0              | 0              |
| Infection                                   |                |                |
| subjects affected / exposed                 | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                           | 0              | 0              |
| Latent tuberculosis                         |                |                |
| subjects affected / exposed                 | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                           | 0              | 0              |
| Molluscum contagiosum                       |                |                |
| subjects affected / exposed                 | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                           | 0              | 0              |
| Nail infection                              |                |                |
| subjects affected / exposed                 | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                           | 0              | 0              |
| Nasal herpes                                |                |                |
| subjects affected / exposed                 | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                           | 0              | 0              |
| Oesophageal candidiasis                     |                |                |
| subjects affected / exposed                 | 0 / 24 (0.00%) | 1 / 12 (8.33%) |
| occurrences (all)                           | 0              | 1              |
| Post procedural infection                   |                |                |
| subjects affected / exposed                 | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                           | 0              | 0              |
| Proctitis herpes                            |                |                |
| subjects affected / exposed                 | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                           | 0              | 0              |
| Pulpitis dental                             |                |                |
| subjects affected / exposed                 | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                           | 0              | 0              |
| Scrotal infection                           |                |                |
| subjects affected / exposed <sup>[20]</sup> | 0 / 16 (0.00%) | 0 / 8 (0.00%)  |
| occurrences (all)                           | 0              | 0              |

|                                             |                |                |  |
|---------------------------------------------|----------------|----------------|--|
| Sialoadenitis                               |                |                |  |
| subjects affected / exposed                 | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)                           | 0              | 0              |  |
| Tinea cruris                                |                |                |  |
| subjects affected / exposed                 | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)                           | 0              | 0              |  |
| Tooth infection                             |                |                |  |
| subjects affected / exposed                 | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)                           | 0              | 0              |  |
| Vaginal infection                           |                |                |  |
| subjects affected / exposed <sup>[21]</sup> | 1 / 8 (12.50%) | 0 / 4 (0.00%)  |  |
| occurrences (all)                           | 1              | 0              |  |
| Viral infection                             |                |                |  |
| subjects affected / exposed                 | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)                           | 0              | 0              |  |
| Alpha haemolytic streptococcal infection    |                |                |  |
| subjects affected / exposed                 | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)                           | 0              | 0              |  |
| COVID-19 pneumonia                          |                |                |  |
| subjects affected / exposed                 | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)                           | 0              | 0              |  |
| Campylobacter infection                     |                |                |  |
| subjects affected / exposed                 | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)                           | 0              | 0              |  |
| Enterocolitis viral                         |                |                |  |
| subjects affected / exposed                 | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)                           | 0              | 0              |  |
| Erysipelas                                  |                |                |  |
| subjects affected / exposed                 | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)                           | 0              | 0              |  |
| Eye infection                               |                |                |  |
| subjects affected / exposed                 | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)                           | 0              | 0              |  |
| Fungal skin infection                       |                |                |  |

|                                  |                |                |
|----------------------------------|----------------|----------------|
| subjects affected / exposed      | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                | 0              | 0              |
| Gastroenteritis norovirus        |                |                |
| subjects affected / exposed      | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                | 0              | 0              |
| Gastroenteritis viral            |                |                |
| subjects affected / exposed      | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                | 0              | 0              |
| Gastrointestinal viral infection |                |                |
| subjects affected / exposed      | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                | 0              | 0              |
| Gingivitis                       |                |                |
| subjects affected / exposed      | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                | 0              | 0              |
| Helicobacter gastritis           |                |                |
| subjects affected / exposed      | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                | 0              | 0              |
| Helicobacter infection           |                |                |
| subjects affected / exposed      | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                | 0              | 0              |
| Herpes simplex                   |                |                |
| subjects affected / exposed      | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                | 0              | 0              |
| Herpes virus infection           |                |                |
| subjects affected / exposed      | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                | 0              | 0              |
| Infected cyst                    |                |                |
| subjects affected / exposed      | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                | 0              | 0              |
| Kidney infection                 |                |                |
| subjects affected / exposed      | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                | 0              | 0              |
| Localised infection              |                |                |
| subjects affected / exposed      | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                | 0              | 0              |
| Measles                          |                |                |

|                             |                |                |  |
|-----------------------------|----------------|----------------|--|
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Moraxella infection         |                |                |  |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Neutropenic sepsis          |                |                |  |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Onychomycosis               |                |                |  |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Ophthalmic herpes simplex   |                |                |  |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Oral fungal infection       |                |                |  |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Periorbital cellulitis      |                |                |  |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Pneumonia haemophilus       |                |                |  |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Pulmonary mycosis           |                |                |  |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Septic shock                |                |                |  |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Skin bacterial infection    |                |                |  |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Splenic infection           |                |                |  |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Staphylococcal sepsis       |                |                |  |

|                                             |                |                |  |
|---------------------------------------------|----------------|----------------|--|
| subjects affected / exposed                 | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)                           | 0              | 0              |  |
| Streptococcal bacteraemia                   |                |                |  |
| subjects affected / exposed                 | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)                           | 0              | 0              |  |
| Tinea pedis                                 |                |                |  |
| subjects affected / exposed                 | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)                           | 0              | 0              |  |
| Tinea versicolour                           |                |                |  |
| subjects affected / exposed                 | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)                           | 0              | 0              |  |
| Urinary tract infection enterococcal        |                |                |  |
| subjects affected / exposed                 | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)                           | 0              | 0              |  |
| Viral pharyngitis                           |                |                |  |
| subjects affected / exposed                 | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)                           | 0              | 0              |  |
| Viral upper respiratory tract infection     |                |                |  |
| subjects affected / exposed                 | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)                           | 0              | 0              |  |
| Vulvovaginal mycotic infection              |                |                |  |
| subjects affected / exposed <sup>[22]</sup> | 0 / 8 (0.00%)  | 0 / 4 (0.00%)  |  |
| occurrences (all)                           | 0              | 0              |  |
| Wound infection                             |                |                |  |
| subjects affected / exposed                 | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)                           | 0              | 0              |  |
| Contusion                                   |                |                |  |
| subjects affected / exposed                 | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)                           | 0              | 0              |  |
| Ligament sprain                             |                |                |  |
| subjects affected / exposed                 | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)                           | 0              | 0              |  |
| Humerus fracture                            |                |                |  |
| subjects affected / exposed                 | 0 / 24 (0.00%) | 1 / 12 (8.33%) |  |
| occurrences (all)                           | 0              | 1              |  |
| Metabolism and nutrition disorders          |                |                |  |

|                             |                |                |
|-----------------------------|----------------|----------------|
| Hypokalaemia                |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Decreased appetite          |                |                |
| subjects affected / exposed | 1 / 24 (4.17%) | 0 / 12 (0.00%) |
| occurrences (all)           | 1              | 0              |
| Hypomagnesaemia             |                |                |
| subjects affected / exposed | 1 / 24 (4.17%) | 0 / 12 (0.00%) |
| occurrences (all)           | 1              | 0              |
| Dehydration                 |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Hypophosphataemia           |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 1 / 12 (8.33%) |
| occurrences (all)           | 0              | 2              |
| Hyponatraemia               |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Hypercalcaemia              |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Hyperglycaemia              |                |                |
| subjects affected / exposed | 1 / 24 (4.17%) | 0 / 12 (0.00%) |
| occurrences (all)           | 1              | 0              |
| Hyperuricaemia              |                |                |
| subjects affected / exposed | 1 / 24 (4.17%) | 0 / 12 (0.00%) |
| occurrences (all)           | 2              | 0              |
| Hypocalcaemia               |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Hypercholesterolaemia       |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Hyperkalaemia               |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |

|                             |                |                |
|-----------------------------|----------------|----------------|
| Tumour lysis syndrome       |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Vitamin D deficiency        |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Gout                        |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Hyperlipidaemia             |                |                |
| subjects affected / exposed | 1 / 24 (4.17%) | 0 / 12 (0.00%) |
| occurrences (all)           | 1              | 0              |
| Hypertriglyceridaemia       |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Hypoalbuminaemia            |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Hypoglycaemia               |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Increased appetite          |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Acidosis                    |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Diabetes mellitus           |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Fluid overload              |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Fluid retention             |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |

|                             |                |                |
|-----------------------------|----------------|----------------|
| Iron deficiency             |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Magnesium deficiency        |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Malnutrition                |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Metabolic acidosis          |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Type 2 diabetes mellitus    |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Abnormal loss of weight     |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Cachexia                    |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Failure to thrive           |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Hypermagnesaemia            |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Hypernatraemia              |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Hyperphosphataemia          |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |
| Hypochloraemia              |                |                |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0              | 0              |

|                             |                |                |  |
|-----------------------------|----------------|----------------|--|
| Hypoproteinaemia            |                |                |  |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Obesity                     |                |                |  |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Vitamin B12 deficiency      |                |                |  |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Zinc deficiency             |                |                |  |
| subjects affected / exposed | 0 / 24 (0.00%) | 0 / 12 (0.00%) |  |
| occurrences (all)           | 0              | 0              |  |
| Myalgia                     |                |                |  |
| subjects affected / exposed | 2 / 24 (8.33%) | 1 / 12 (8.33%) |  |
| occurrences (all)           | 3              | 1              |  |
| Neck pain                   |                |                |  |
| subjects affected / exposed | 1 / 24 (4.17%) | 0 / 12 (0.00%) |  |
| occurrences (all)           | 1              | 0              |  |

Notes:

[3] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: Number of subjects exposed to this adverse event term is based on the male population in this study.

[4] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: Number of subjects exposed to this adverse event term is based on the female population in this study.

[5] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: Number of subjects exposed to this adverse event term is based on the male population in this study.

[6] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: Number of subjects exposed to this adverse event term is based on the female population in this study.

[7] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: Number of subjects exposed to this adverse event term is based on the female population in this study.

[8] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: Number of subjects exposed to this adverse event term is based on the female population in this study.

[9] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: Number of subjects exposed to this adverse event term is based on the female population in this study.

[10] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: Number of subjects exposed to this adverse event term is based on the female population

in this study.

[11] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: Number of subjects exposed to this adverse event term is based on the male population in this study.

[12] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: Number of subjects exposed to this adverse event term is based on the female population in this study.

[13] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: Number of subjects exposed to this adverse event term is based on the male population in this study.

[14] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: Number of subjects exposed to this adverse event term is based on the male population in this study.

[15] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: Number of subjects exposed to this adverse event term is based on the male population in this study.

[16] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: Number of subjects exposed to this adverse event term is based on the male population in this study.

[17] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: Number of subjects exposed to this adverse event term is based on the female population in this study.

[18] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: Number of subjects exposed to this adverse event term is based on the female population in this study.

[19] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: Number of subjects exposed to this adverse event term is based on the female population in this study.

[20] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: Number of subjects exposed to this adverse event term is based on the male population in this study.

[21] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: Number of subjects exposed to this adverse event term is based on the female population in this study.

[22] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: Number of subjects exposed to this adverse event term is based on the female population in this study.

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date            | Amendment                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |
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| 25 August 2016  | <p>All subjects are now required to start prophylaxis treatment with pneumocystis jiroveci pneumonia (PCP) and antiviral therapy within 7 days prior to randomisation, whereas this was previously at investigator discretion. The phrasing of response assessment intervals has been revised for clarity from "on weeks 8,16, and 24, and then every 12 weeks thereafter," to "at the end of Cycles 2, 4, and 6, and then every 3 cycles thereafter". The shelf life of ublituximab has been increased to 36 months from 24 months when stored between +2 C / +8 C to reflect newly available stability data on ublituximab drug product. The tissue sample requirements at screening were revised for subjects with previous documentation of DLBCL subtype. For these subjects, tissue can now be submitted within +/-30 days of Day 1 of Cycle 1. If no documentation of DLBCL subtype is available prior to screening, a tissue sample must be submitted during the screening period to allow for central determination of DLBCL subtype prior to randomisation.</p> <p>Updated to include the most recent AE information related to ublituximab and TGR-1202 corresponding to the latest Investigator's Brochures.</p>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
| 15 January 2017 | <p>Women of childbearing potential were required to undergo monthly urine pregnancy testing beginning in Cycle 2.</p>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |
| 12 April 2017   | <p>Additional cohorts were added, and eligibility criteria were expanded to allow enrolment of subjects with the following indolent types of NHL: FL, SLL, and MZL. Arm C was added to evaluate the combination of TGR-1202, ublituximab, and bendamustine in subjects with DLBCL and those with FL or SLL. Stratification by DLBCL subtype prior to randomisation was removed, however archived tissue for central determination of DLBCL subtype is still required within 30 days of Day 1 of Cycle 1. Number of subjects was expanded- up to approximately 400 subjects with DLBCL, up to approximately 400 subjects with FL or SLL, and up to approximately 60 subjects with MZL, provided no arms are closed for futility or at planned interim analyses. The number of potential study centres was expanded from up to 100 to up to 150, and the timeframe for enrolment was expanded from up to 14 months to up to 36 months. The window for use of medically acceptable methods of contraception for female subjects of child-bearing potential and male partners was expanded from throughout the study period and for 30 days after the last dose of either study drug to throughout the study period and for 4 months after the last dose of either study drug. Exclusion criteria 1, 3, 4,5, and 9 were updated. The response assessment schedule was revised from at the end of Cycles 2, 4, and 6 and then every 3 cycles thereafter, to during Cycles 3 and 6, and then every 3 cycles thereafter. The window for tumour evaluations was expanded from +/- 7 days to +/- 14 days. The screening period was expanded from 21 days to 28 days. Unilateral bone marrow aspirate and/or biopsy was only needed postbaseline to confirm a CR in subjects with marrow involvement at baseline and without FDG-avid disease. PET scans were previously required at baseline and routinely in subjects with FDG-avid disease. Study Assessment Table was amended and a second assessment table for subjects on the ublituximab+TGR-1202+bendamustine regimen added.</p> |

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| 01 October 2017  | <p>Provided additional justification for the study of TGR-1202 monotherapy in subjects with MZL. Inclusion criterion 1(d), 2(a), 4(d) and exclusion criterion 9(c) were modified. The FL/SLL cohort was modified to include a Stage 1 to evaluate TGR-1202 monotherapy in up to 150 subjects prior to proceeding to Stage 2 which will randomise subjects to either TGR-1202 alone or in combination with ublituximab. The schedule for response evaluation previously stated to evaluate response "during" Cycles 3 and 6 and then every 3 cycles thereafter and was clarified to evaluate response "at the end of Cycle 3 and then within 14 days prior to Cycle 6, Day 1, and every 3 cycles thereafter (9, 12, etc.)". The study assessment tables were updated to specify that bone marrow aspirate and/or biopsy was optional only for subjects with DLBCL and required for subjects with FL, SLL, and MZL. Updated to include sparse sampling for population pharmacokinetics from all enrolled subjects, not just subjects in the DLBCL cohort, and the sparse sampling instructions were clarified. Updated to include information regarding a new vial size for ublituximab. Updated to clarify that pre-medications for bendamustine are recommended but optional and per institutional standard of care, which should at least include use of a corticosteroid, and that use of prophylactic growth factor support is allowed. Provided more specific instructions around dose-modifications in the event of diarrhoea and/or colitis. Reference to an interim analysis in the FL/SLL cohort was removed. Futility-stopping rules were added for the MZL cohort and the FL/SLL cohort based on Simon's 2-stage design.</p> |
| 15 February 2018 | <p>The number of trial sites was expanded from 150 to 200 sites. A cohort of subjects with MCL was added to the study, affecting the following sections: Primary objectives: amended to include efficacy objectives for MCL subjects; inclusion criteria 1, 2 and exclusion criteria 7, 8 were amended. Enrolment to Arm A of the DLBCL Cohort was suspended following accrual of a sufficient number of subjects. The schedule for response evaluation previously stated to evaluate response "at the end of Cycle 3 and then within 14 days prior to Cycle 6, Day 1, and every 3 cycles thereafter (9, 12, etc.)" and was amended to evaluate response, "at the end of Cycle 3 and then within 14 days prior to day 1 of Cycles 6, 9, and 12. After Cycle 12, response assessments should occur every 6 cycles or more frequently.". Amended to include background information and rationale for the addition of MCL subjects to this study. Modified to provide dose delay and/or modification guidelines for bendamustine for subjects experiencing occurrence of neutropenic fever or infection. The risk profile of ublituximab and TGR-1202 was updated to reflect the most recent safety data available from each agent. Other minor clarifications and administrative updates were made.</p>                                                                                                                                                                                                                                                                                                                                                                                                                                  |
| 20 August 2018   | <p>The primary objectives of the study were re-written to reflect ORR as the primary endpoint for all cohorts. The key secondary objectives of CR rate for subjects with FL or SLL and PFS for subjects with DLBCL were revised to be Secondary Objectives. Inclusion Criterion 2 was amended. Stage 2 of the FL and SLL cohort was revised as follows: Stage 2 will only enrol subjects with FL, and no longer will enrol SLL, subjects will be randomised in a 3:1:1 ratio to receive ublituximab + TGR-1202 (Arm A), TGR-1202 monotherapy (Arm B), or ublituximab monotherapy (Arm D), subjects randomised to Arm D with documented progression will be eligible to cross-over to receive TGR-1202 monotherapy. Stage 2 of the MZL cohort was added to enrol an additional 60 subjects to receive the combination of ublituximab + TGR-1202. The duration of ublituximab therapy was truncated to stop at the end of Cycle 24 for any ublituximab-containing arm. Guidelines for holding anti-hypertensive medications during ublituximab infusions were updated. Eligibility for subjects with DLBCL was removed based on completion of target enrolment in the DLBCL cohorts. Statistical assumptions for the MZL, FL/SLL, and DLBCL cohorts were revised in accordance with recent Statistical Analysis Plans. Updated to provide further information on preferred PCP prophylactic agents. Updated to include the most recent AE information related to ublituximab and TGR-1202 corresponding to the latest Investigator's Brochures. Minor administrative updates and typographical errors were corrected throughout.</p>                                                                                                     |

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| 20 September 2018 | Inclusion Criterion 2C for subjects with MCL was clarified to state that the prior BTK inhibitor requirement is limited to only ibrutinib or acalabrutinib. Exclusion Criterion 1 was updated to allow palliative radiation therapy during the 21-day period prior to Day 1 of Cycle 1. Updated to include cytomegalovirus (CMV) surveillance for all subjects. Amended to provide additional guidance for ublituximab pre-medications. Revised to allow dose delays of any study medication for durations longer than 28 days to recover from toxicity. All dose modifications should now be reported in the Interactive Web Response System (IWRS), with questions regarding dose modifications referred to TG Therapeutics. Updated to provide clarification on the liver toxicity dose modification guidelines. Updated to include a cut-off date for the safety information for ublituximab and umbralisib. The latest safety information for each study drug is contained in the most recent investigator's brochures. Administrative updates and typographical errors were corrected throughout, including the changing of terminology from "patient" to "subject" and the inclusion of the generic name for "umbralisib" for TGR-1202.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| 19 November 2020  | Cover page updated to add medical monitor and update study chair information. Eligibility criteria inclusion 1 updated to note that DLBCL is no longer enrolling, however subjects with SLL are eligible for enrolment. Eligibility criteria inclusion 2 updated to include FL, SLL, and MZL subjects that are treatment naïve or previously treated are now eligible. FL subjects are no longer required to be relapsed or refractory after $\geq 2$ prior lines of systemic therapy, nor does the requirement to have received an anti-CD20 monoclonal antibody (mAb) and an alkylating agent apply. MZL subjects are no longer required to have prior treatment with one or more lines of prior treatment including at least one CD20-directed regimen (either as monotherapy or as chemoimmunotherapy) with documented failure to achieve at least PR or documented PD after the most recent systemic treatment regimen. Exclusion criteria 3 updated to clarify evidence of chronic active HBV is a detectable hepatitis b surface antigen. Updated to include a Stage 3 to include new dosing cohorts for subjects with FL, SLL or MZL. Ublituximab 36 milliliter per 900 mg vials are now available, protocol updated throughout to reflect the updated vials size, stability information, and dilution instructions. The storage of ublituximab if diluted in polyolefin (PO) infusion bags and lines can be extended to 48 hours refrigerated. Stage 3 enrolment and sample size added. Sparse Sampling PK added for subjects enrolled to Stage 3. Added to clarify umbralisib dosing cohorts in Stage 3. Updated to add details on crossover from Arm D to Arm B. Information on scheduling of ublituximab pre-medications for potential infusion related reactions (IRR) updated to be more clear, information on prophylaxis with antiviral agents for hepatitis B added for subjects with a prior history of hepatitis B and for those with a positive anti-HBc with negative HBsAg at screening. Updated contact information for any product quality complaint. |

Notes:

## Interruptions (globally)

Were there any global interruptions to the trial? No

## Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Sponsor opted to terminate the study due to business decision.

Notes: