



## Clinical trial results:

**An open label, Phase Ia/Ib dose finding study with BI 894999 orally administered once a day in patients with advanced malignancies with repeated administration in patients with clinical benefit**

### Summary

|                          |                  |
|--------------------------|------------------|
| EudraCT number           | 2015-001111-12   |
| Trial protocol           | BE DE DK         |
| Global end of trial date | 23 November 2021 |

### Results information

|                                |                  |
|--------------------------------|------------------|
| Result version number          | v2 (current)     |
| This version publication date  | 30 May 2024      |
| First version publication date | 15 December 2022 |
| Version creation reason        |                  |

### Trial information

#### Trial identification

|                       |        |
|-----------------------|--------|
| Sponsor protocol code | 1367.1 |
|-----------------------|--------|

#### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT02516553 |
| WHO universal trial number (UTN)   | -           |

Notes:

### Sponsors

|                              |  |
|------------------------------|--|
| Sponsor organisation name    | Boehringer Ingelheim   |
| Sponsor organisation address | Binger Strasse 173, Ingelheim am Rhein, Germany, 55216   |
| Public contact               | Boehringer Ingelheim, Call Center, Boehringer Ingelheim, 001 18002430127, <a href="mailto:clintriage.rdg@boehringer-ingelheim.com">clintriage.rdg@boehringer-ingelheim.com</a> |
| Scientific contact           | Boehringer Ingelheim, Call Center, Boehringer Ingelheim, 001 18002430127, <a href="mailto:clintriage.rdg@boehringer-ingelheim.com">clintriage.rdg@boehringer-ingelheim.com</a> |

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                       | 31 January 2022  |
| Is this the analysis of the primary completion data? | Yes              |
| Primary completion date                              | 23 November 2021 |
| Global end of trial reached?                         | Yes              |
| Global end of trial date                             | 23 November 2021 |
| Was the trial ended prematurely?                     | No               |

Notes:

## General information about the trial

Main objective of the trial:

The trial comprised a dose escalation phase (Phase Ia) and an expansion phase (Phase Ib). The main objective of this trial part was to determine the maximum tolerated dose (MTD) of BI 894999 monotherapy in patients with advanced and/or metastatic solid tumours in different dosing schedules in 3- or 4-week cycles (Schedule A with continuous dosing, Schedule B, with intermittent dosing [2 weeks on treatment, 1 week off treatment in 3-week cycles]; Schedule C, with intermittent dosing [a loading dose on first day followed by a maintenance dose for the next 6 days and followed by 1 week off treatment, repeated every 2 weeks in 4-week cycles]).

Protection of trial subjects:

Only subjects that met all the study inclusion and none of the exclusion criteria were to be entered in the study. All subjects were free to withdraw from the clinical trial at any time for any reason given. If a subject continued to take trial medication, close monitoring was adhered to and all adverse events recorded. Rules were implemented in all trials whereby doses would be reduced if required. Thereafter, if further events were reported, the subject would be withdrawn from the trial. Symptomatic treatment of tumour associated symptoms were allowed throughout.

Background therapy: -

Evidence for comparator: -

|   |              |
|---|--------------|
| Actual start date of recruitment                          | 20 July 2015 |
| Long term follow-up planned                               | No           |
| Independent data monitoring committee (IDMC) involvement? | Yes          |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |                       |
|--------------------------------------|-----------------------|
| Country: Number of subjects enrolled | Belgium: 137          |
| Country: Number of subjects enrolled | France: 42            |
| Country: Number of subjects enrolled | Germany: 19           |
| Country: Number of subjects enrolled | Korea, Republic of: 1 |
| Country: Number of subjects enrolled | Spain: 4              |
| Country: Number of subjects enrolled | United States: 28     |
| Worldwide total number of subjects   | 231                   |
| EEA total number of subjects         | 202                   |

Notes:

### Subjects enrolled per age group

|          |   |
|----------|---|
| In utero | 0 |
|----------|---|

|   |     |
|---|-----|
| Preterm newborn - gestational age < 37 wk | 0   |
| Newborns (0-27 days)                      | 0   |
| Infants and toddlers (28 days-23 months)  | 0   |
| Children (2-11 years)                     | 0   |
| Adolescents (12-17 years)                 | 0   |
| Adults (18-64 years)                      | 138 |
| From 65 to 84 years                       | 88  |
| 85 years and over                         | 5   |

## Subject disposition

### Recruitment

Recruitment details:

This was an open label, Phase Ia/Ib dose finding study with BI 894999 orally administered once a day in patients with advanced malignancies with repeated administration in patients with clinical benefit.

### Pre-assignment

Screening details:

For Phase Ib-Schedule B SCLC, Phase Ib-Schedule B mCRPC, DMC lowered the dose of SCLC and mCRPC, thus patients treated prior the decision took 2.5mg BI 894999 and patients treated after the decision received 2mg . For Phase Ib - Schedule C NC, the dose was lowered since DMC reclaimed the MTD as 6/3mg after 1 patient already treated with 7/3.5mg.

### Period 1

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

Blinding implementation details:

This was an open-label trial.

### Arms

|                              |   |
|------------------------------|---|
| Are arms mutually exclusive? | Yes                                     |
| <b>Arm title</b>             | Phase Ia - Schedule A: 0.2 mg BI 894999 |

Arm description:

Adult patients with a confirmed diagnosis of advanced, unresectable and/or metastatic malignant solid tumours who had failed conventional treatment or for whom no therapy of proven efficacy existed or who were not amenable to standard therapies were administered orally 0.2 milligram (mg) of BI 894999 once daily, in the morning, after an overnight fast, 1 hour before breakfast with at least 250 milliliter (mL) of water. Schedule A was a continuous daily intake in cycles of 21 days.

|  |                    |
|--|--------------------|
| Arm type                               | Experimental       |
| Investigational medicinal product name | BI 894999          |
| Investigational medicinal product code |                    |
| Other name                             |                    |
| Pharmaceutical forms                   | Film-coated tablet |
| Routes of administration               | Oral use           |

Dosage and administration details:

Patients were administered orally 0.2 milligram (mg) of BI 894999 once daily, in the morning, after an overnight fast, 1 hour before breakfast with at least 250 milliliter (mL) of water. Schedule A was a continuous daily intake in cycles of 21 days.

|                  |   |
|------------------|---|
| <b>Arm title</b> | Phase Ia - Schedule A: 0.5 mg BI 894999 |
|------------------|---|

Arm description:

Adult patients with a confirmed diagnosis of advanced, unresectable and/or metastatic malignant solid tumours who had failed conventional treatment or for whom no therapy of proven efficacy existed or who were not amenable to standard therapies were administered orally 0.5 milligram (mg) of BI 894999 once daily, in the morning, after an overnight fast, 1 hour before breakfast with at least 250 milliliter (mL) of water. Schedule A was a continuous daily intake in cycles of 21 days.

|  |                    |
|--|--------------------|
| Arm type                               | Experimental       |
| Investigational medicinal product name | BI 894999          |
| Investigational medicinal product code |                    |
| Other name                             |                    |
| Pharmaceutical forms                   | Film-coated tablet |
| Routes of administration               | Oral use           |

Dosage and administration details:

Patients were administered orally 0.5 milligram (mg) of BI 894999 once daily, in the morning, after an

overnight fast, 1 hour before breakfast with at least 250 milliliter (mL) of water. Schedule A was a continuous daily intake in cycles of 21 days.

|   |                                       |
|---|---------------------------------------|
| <b>Arm title</b>  | Phase Ia - Schedule A: 1 mg BI 894999 |
| Arm description:<br>Adult patients with a confirmed diagnosis of advanced, unresectable and/or metastatic malignant solid tumours who had failed conventional treatment or for whom no therapy of proven efficacy existed or who were not amenable to standard therapies were administered orally 1 milligram (mg) of BI 894999 once daily, in the morning, after an overnight fast, 1 hour before breakfast with at least 250 milliliter (mL) of water. Schedule A was a continuous daily intake in cycles of 21 days. |                                       |
| Arm type  | Experimental                          |
| Investigational medicinal product name  | BI 894999                             |
| Investigational medicinal product code  |                                       |
| Other name  |                                       |
| Pharmaceutical forms  | Film-coated tablet                    |
| Routes of administration  | Oral use                              |

**Dosage and administration details:**

Patients were administered orally 1 milligram (mg) of BI 894999 once daily, in the morning, after an overnight fast, 1 hour before breakfast with at least 250 milliliter (mL) of water. Schedule A was a continuous daily intake in cycles of 21 days.

|   |   |
|---|---|
| <b>Arm title</b>  | Phase Ia - Schedule A: 1.5 mg BI 894999 |
| Arm description:<br>Adult patients with a confirmed diagnosis of advanced, unresectable and/or metastatic malignant solid tumours who had failed conventional treatment or for whom no therapy of proven efficacy existed or who were not amenable to standard therapies were administered orally 1.5 milligram (mg) of BI 894999 once daily, in the morning, after an overnight fast, 1 hour before breakfast with at least 250 milliliter (mL) of water. Schedule A was a continuous daily intake in cycles of 21 days. |   |
| Arm type  | Experimental                            |
| Investigational medicinal product name  | BI 894999                               |
| Investigational medicinal product code  |   |
| Other name  |   |
| Pharmaceutical forms  | Film-coated tablet                      |
| Routes of administration  | Oral use                                |

**Dosage and administration details:**

Patients were administered orally 1.5 milligram (mg) of BI 894999 once daily, in the morning, after an overnight fast, 1 hour before breakfast with at least 250 milliliter (mL) of water. Schedule A was a continuous daily intake in cycles of 21 days.

|   |                                       |
|---|---------------------------------------|
| <b>Arm title</b>  | Phase Ia - Schedule A: 2 mg BI 894999 |
| Arm description:<br>Adult patients with a confirmed diagnosis of advanced, unresectable and/or metastatic malignant solid tumours who had failed conventional treatment or for whom no therapy of proven efficacy existed or who were not amenable to standard therapies were administered orally 2 milligram (mg) of BI 894999 once daily, in the morning, after an overnight fast, 1 hour before breakfast with at least 250 milliliter (mL) of water. Schedule A was a continuous daily intake in cycles of 21 days. |                                       |
| Arm type  | Experimental                          |
| Investigational medicinal product name  | BI 894999                             |
| Investigational medicinal product code  |                                       |
| Other name  |                                       |
| Pharmaceutical forms  | Film-coated tablet                    |
| Routes of administration  | Oral use                              |

**Dosage and administration details:**

Patients were administered orally 2 milligram (mg) of BI 894999 once daily, in the morning, after an overnight fast, 1 hour before breakfast with at least 250 milliliter (mL) of water. Schedule A was a

continuous daily intake in cycles of 21 days.

|   |                                       |
|---|---------------------------------------|
| <b>Arm title</b>  | Phase Ia - Schedule A: 5 mg BI 894999 |
| Arm description:<br>Adult patients with a confirmed diagnosis of advanced, unresectable and/or metastatic malignant solid tumours who had failed conventional treatment or for whom no therapy of proven efficacy existed or who were not amenable to standard therapies were administered orally 5 milligram (mg) of BI 894999 once daily, in the morning, after an overnight fast, 1 hour before breakfast with at least 250 milliliter (mL) of water. Schedule A was a continuous daily intake in cycles of 21 days. |                                       |
| Arm type  | Experimental                          |
| Investigational medicinal product name  | BI 894999                             |
| Investigational medicinal product code  |                                       |
| Other name  |                                       |
| Pharmaceutical forms  | Film-coated tablet                    |
| Routes of administration  | Oral use                              |

**Dosage and administration details:**

Patients were administered orally 5 milligram (mg) of BI 894999 once daily, in the morning, after an overnight fast, 1 hour before breakfast with at least 250 milliliter (mL) of water. Schedule A was a continuous daily intake in cycles of 21 days.

|  |   |
|--|---|
| <b>Arm title</b>   | Phase Ia - Schedule B: 1.5 mg BI 894999 |
| Arm description:<br>Adult patients with a confirmed diagnosis of advanced, unresectable and/or metastatic malignant solid tumours who had failed conventional treatment or for whom no therapy of proven efficacy existed or who were not amenable to standard therapies were administered orally 1.5 milligram (mg) of BI 894999 once daily, in the morning, after an overnight fast, 1 hour before breakfast with at least 250 milliliter (mL) of water. Schedule B was a continuous intake for 14 days followed by one week off treatment in cycles of 21 days. |   |
| Arm type   | Experimental                            |
| Investigational medicinal product name   | BI 894999                               |
| Investigational medicinal product code   |   |
| Other name   |   |
| Pharmaceutical forms   | Film-coated tablet                      |
| Routes of administration   | Oral use                                |

**Dosage and administration details:**

Patients were administered orally 1.5 milligram (mg) of BI 894999 once daily, in the morning, after an overnight fast, 1 hour before breakfast with at least 250 milliliter (mL) of water. Schedule B was a continuous intake for 14 days followed by one week off treatment in cycles of 21 days.

|  |                                       |
|--|---------------------------------------|
| <b>Arm title</b>   | Phase Ia - Schedule B: 2 mg BI 894999 |
| Arm description:<br>Adult patients with a confirmed diagnosis of advanced, unresectable and/or metastatic malignant solid tumours who had failed conventional treatment or for whom no therapy of proven efficacy existed or who were not amenable to standard therapies were administered orally 2 milligram (mg) of BI 894999 once daily, in the morning, after an overnight fast, 1 hour before breakfast with at least 250 milliliter (mL) of water. Schedule B was a continuous intake for 14 days followed by one week off treatment in cycles of 21 days. |                                       |
| Arm type   | Experimental                          |
| Investigational medicinal product name   | BI 894999                             |
| Investigational medicinal product code   |                                       |
| Other name   |                                       |
| Pharmaceutical forms   | Film-coated tablet                    |
| Routes of administration   | Oral use                              |

**Dosage and administration details:**

Patients were administered orally 2 milligram (mg) of BI 894999 once daily, in the morning, after an overnight fast, 1 hour before breakfast with at least 250 milliliter (mL) of water. Schedule B was a continuous intake for 14 days followed by one week off treatment in cycles of 21 days.

|                  |   |
|------------------|---|
| <b>Arm title</b> | Phase Ia - Schedule B: 2.5 mg BI 894999 |
|------------------|---|

**Arm description:**

Adult patients with a confirmed diagnosis of advanced, unresectable and/or metastatic malignant solid tumours who had failed conventional treatment or for whom no therapy of proven efficacy existed or who were not amenable to standard therapies were administered orally 2.5 mg of BI 894999 once daily, in the morning, after an overnight fast, 1 hour before breakfast with at least 250 milliliter (mL) of water. Schedule B was a continuous intake for 14 days followed by one week off treatment in cycles of 21 days.

|  |                    |
|--|--------------------|
| Arm type                               | Experimental       |
| Investigational medicinal product name | BI 894999          |
| Investigational medicinal product code |                    |
| Other name                             |                    |
| Pharmaceutical forms                   | Film-coated tablet |
| Routes of administration               | Oral use           |

**Dosage and administration details:**

Patients were administered orally 2.5 milligram (mg) of BI 894999 once daily, in the morning, after an overnight fast, 1 hour before breakfast with at least 250 milliliter (mL) of water. Schedule B was a continuous intake for 14 days followed by one week off treatment in cycles of 21 days.

|                  |   |
|------------------|---|
| <b>Arm title</b> | Phase Ia - Schedule C: 5/2.5 mg BI 894999 |
|------------------|---|

**Arm description:**

Adult patients with a confirmed diagnosis of advanced, unresectable and/or metastatic malignant solid tumours who had failed conventional treatment or for whom no therapy of proven efficacy existed or who were not amenable to standard therapies were administered orally once daily on Day 1 and on Day 15 of each cycle a loading dose of 5 milligram (mg) of BI 894999, followed by six days daily intake of the maintenance dose of 2.5 mg of BI 894999 once daily, followed by one week off, repeated every two weeks in cycles of 28 days (Schedule C). The loading and the maintenance dose were administered in the morning, after an overnight fast, 1 hour before breakfast with at least 250 milliliter (mL) of water.

|  |                    |
|--|--------------------|
| Arm type                               | Experimental       |
| Investigational medicinal product name | BI 894999          |
| Investigational medicinal product code |                    |
| Other name                             |                    |
| Pharmaceutical forms                   | Film-coated tablet |
| Routes of administration               | Oral use           |

**Dosage and administration details:**

Patients were administered orally once daily on Day 1 and on Day 15 of each cycle a loading dose of 5 milligram (mg) of BI 894999, followed by six days daily intake of the maintenance dose of 2.5 mg of BI 894999 once daily, followed by one week off, repeated every two weeks in cycles of 28 days (Schedule C). The loading and the maintenance dose were administered in the morning, after an overnight fast, 1 hour before breakfast with at least 250 milliliter (mL) of water.

|                  |   |
|------------------|---|
| <b>Arm title</b> | Phase Ia - Schedule C: 6/3 mg BI 894999 |
|------------------|---|

**Arm description:**

Adult patients with a confirmed diagnosis of advanced, unresectable and/or metastatic malignant solid tumours who had failed conventional treatment or for whom no therapy of proven efficacy existed or who were not amenable to standard therapies were administered orally once daily on Day 1 and on Day 15 of each cycle a loading dose of 6 milligram (mg) of BI 894999, followed by six days daily intake of the maintenance dose of 3 mg of BI 894999 once daily, followed by one week off, repeated every two weeks in cycles of 28 days (Schedule C). The loading and the maintenance dose were administered in the morning, after an overnight fast, 1 hour before breakfast with at least 250 milliliter (mL) of water.

|          |              |
|----------|--------------|
| Arm type | Experimental |
|----------|--------------|

|  |                    |
|--|--------------------|
| Investigational medicinal product name | BI 894999          |
| Investigational medicinal product code |                    |
| Other name                             |                    |
| Pharmaceutical forms                   | Film-coated tablet |
| Routes of administration               | Oral use           |

**Dosage and administration details:**

Patients were administered orally once daily on Day 1 and on Day 15 of each cycle a loading dose of 6 milligram (mg) of BI 894999, followed by six days daily intake of the maintenance dose of 3 mg of BI 894999 once daily, followed by one week off, repeated every two weeks in cycles of 28 days (Schedule C). The loading and the maintenance dose were administered in the morning, after an overnight fast, 1 hour before breakfast with at least 250 milliliter (mL) of water.

|                  |   |
|------------------|---|
| <b>Arm title</b> | Phase Ia - Schedule C: 7/3.5 mg BI 894999 |
|------------------|---|

**Arm description:**

Adult patients with a confirmed diagnosis of advanced, unresectable and/or metastatic malignant solid tumours who had failed conventional treatment or for whom no therapy of proven efficacy existed or who were not amenable to standard therapies were administered orally once daily on Day 1 and on Day 15 of each cycle a loading dose of 7 milligram (mg) of BI 894999, followed by six days daily intake of the maintenance dose of 3.5 mg of BI 894999 once daily, followed by one week off, repeated every two weeks in cycles of 28 days (Schedule C). The loading and the maintenance dose were administered in the morning, after an overnight fast, 1 hour before breakfast with at least 250 milliliter (mL) of water.

|  |                    |
|--|--------------------|
| Arm type                               | Experimental       |
| Investigational medicinal product name | BI 894999          |
| Investigational medicinal product code |                    |
| Other name                             |                    |
| Pharmaceutical forms                   | Film-coated tablet |
| Routes of administration               | Oral use           |

**Dosage and administration details:**

Patients were administered orally once daily on Day 1 and on Day 15 of each cycle a loading dose of 7 milligram (mg) of BI 894999, followed by six days daily intake of the maintenance dose of 3.5 mg of BI 894999 once daily, followed by one week off, repeated every two weeks in cycles of 28 days (Schedule C). The loading and the maintenance dose were administered in the morning, after an overnight fast, 1 hour before breakfast with at least 250 milliliter (mL) of water.

|                  |  |
|------------------|--|
| <b>Arm title</b> | Phase Ia - Schedule B: 1.5 mg BI 894999 (DLBCL patients) |
|------------------|--|

**Arm description:**

Adult patients with histologically confirmed diagnosis of diffuse large B-cell lymphoma (DLBCL) were administered orally 1.5 milligram (mg) of BI 894999 once daily, in the morning, after an overnight fast, 1 hour before breakfast with at least 250 milliliter (mL) of water. Schedule B was a continuous intake for 14 days followed by one week off treatment in cycles of 21 days.

|  |                    |
|--|--------------------|
| Arm type                               | Experimental       |
| Investigational medicinal product name | BI 894999          |
| Investigational medicinal product code |                    |
| Other name                             |                    |
| Pharmaceutical forms                   | Film-coated tablet |
| Routes of administration               | Oral use           |

**Dosage and administration details:**

Patients were administered orally 1.5 milligram (mg) of BI 894999 once daily, in the morning, after an overnight fast, 1 hour before breakfast with at least 250 milliliter (mL) of water. Schedule B was a continuous intake for 14 days followed by one week off treatment in cycles of 21 days.

|                  |  |
|------------------|--|
| <b>Arm title</b> | Phase Ia - Schedule B: 2 mg BI 894999 (DLBCL patients) |
|------------------|--|

**Arm description:**

Adult patients with histologically confirmed diagnosis of diffuse large B-cell lymphoma (DLBCL) were administered orally 2 milligram (mg) of BI 894999 once daily, in the morning, after an overnight fast, 1 hour before breakfast with at least 250 milliliter (mL) of water. Schedule B was a continuous intake for 14 days followed by one week off treatment in cycles of 21 days.

|          |              |
|----------|--------------|
| Arm type | Experimental |
|----------|--------------|



|  |                    |
|--|--------------------|
| Investigational medicinal product name | BI 894999          |
| Investigational medicinal product code |                    |
| Other name                             |                    |
| Pharmaceutical forms                   | Film-coated tablet |
| Routes of administration               | Oral use           |

**Dosage and administration details:**

Patients were administered orally 2 milligram (mg) of BI 894999 once daily, in the morning, after an overnight fast, 1 hour before breakfast with at least 250 milliliter (mL) of water. Schedule B was a continuous intake for 14 days followed by one week off treatment in cycles of 21 days.

|                  |  |
|------------------|--|
| <b>Arm title</b> | Phase Ia - Schedule B: 2.5 mg BI 894999 (DLBCL patients) |
|------------------|--|

**Arm description:**

Adult patients with histologically confirmed diagnosis of diffuse large B-cell lymphoma (DLBCL) were administered orally 2.5 milligram (mg) of BI 894999 once daily, in the morning, after an overnight fast, 1 hour before breakfast with at least 250 milliliter (mL) of water. Schedule B was a continuous intake for 14 days followed by one week off treatment in cycles of 21 days.

|  |                    |
|--|--------------------|
| Arm type                               | Experimental       |
| Investigational medicinal product name | BI 894999          |
| Investigational medicinal product code |                    |
| Other name                             |                    |
| Pharmaceutical forms                   | Film-coated tablet |
| Routes of administration               | Oral use           |

**Dosage and administration details:**

Patients were administered orally 2.5 milligram (mg) of BI 894999 once daily, in the morning, after an overnight fast, 1 hour before breakfast with at least 250 milliliter (mL) of water. Schedule B was a continuous intake for 14 days followed by one week off treatment in cycles of 21 days.

|                  |  |
|------------------|--|
| <b>Arm title</b> | Phase Ia - Schedule C: 4/2 mg BI 894999 (DLBCL patients) |
|------------------|--|

**Arm description:**

Adult patients with histologically confirmed diagnosis of diffuse large B-cell lymphoma (DLBCL) were administered orally once daily on Day 1 and on Day 15 of each cycle a loading dose of 4 milligram (mg) of BI 894999, followed by six days daily intake of the maintenance dose of 2 mg of BI 894999 once daily, followed by one week off, repeated every two weeks in cycles of 28 days (Schedule C). The loading and the maintenance dose were administered in the morning, after an overnight fast, 1 hour before breakfast with at least 250 milliliter (mL) of water.

|  |                    |
|--|--------------------|
| Arm type                               | Experimental       |
| Investigational medicinal product name | BI 894999          |
| Investigational medicinal product code |                    |
| Other name                             |                    |
| Pharmaceutical forms                   | Film-coated tablet |
| Routes of administration               | Oral use           |

**Dosage and administration details:**

Patients were administered orally once daily on Day 1 and on Day 15 of each cycle a loading dose of 4 milligram (mg) of BI 894999, followed by six days daily intake of the maintenance dose of 2 mg of BI 894999 once daily, followed by one week off, repeated every two weeks in cycles of 28 days (Schedule C). The loading and the maintenance dose were administered in the morning, after an overnight fast, 1 hour before breakfast with at least 250 milliliter (mL) of water.

|                  |  |
|------------------|--|
| <b>Arm title</b> | Phase Ia - Schedule C: BI 894999 5/2.5 mg (DLBCL patients) |
|------------------|--|

**Arm description:**

Adult patients with histologically confirmed diagnosis of diffuse large B-cell lymphoma (DLBCL) were administered orally once daily on Day 1 and on Day 15 of each cycle a loading dose of 5 milligram (mg) of BI 894999, followed by six days daily intake of the maintenance dose of 2.5 mg of BI 894999, followed by one week off, repeated every two weeks in cycles of 28 days (Schedule C). The loading and the maintenance dose were administered in the morning, after an overnight fast, 1 hour before breakfast with at least 250 milliliter (mL) of water.

|          |              |
|----------|--------------|
| Arm type | Experimental |
|----------|--------------|

|  |                    |
|--|--------------------|
| Investigational medicinal product name | BI 894999          |
| Investigational medicinal product code |                    |
| Other name                             |                    |
| Pharmaceutical forms                   | Film-coated tablet |
| Routes of administration               | Oral use           |

**Dosage and administration details:**

Patients were administered orally once daily on Day 1 and on Day 15 of each cycle a loading dose of 5 milligram (mg) of BI 894999, followed by six days daily intake of the maintenance dose of 2.5 mg of BI 894999, followed by one week off, repeated every two weeks in cycles of 28 days (Schedule C). The loading and the maintenance dose were administered in the morning, after an overnight fast, 1 hour before breakfast with at least 250 milliliter (mL) of water.

|                  |  |
|------------------|--|
| <b>Arm title</b> | Phase Ib - Schedule B: 2 or 2.5 mg BI 894999 (SCLC patients) |
|------------------|--|

**Arm description:**

This arm included adult patients diagnosed with small cell lung cancer (SCLC).

SCLC patients were initially administered 2.5 mg of BI 894999. BI 894999 administration was performed in the morning, after an overnight fast, 1 hour before breakfast with at least 250 milliliter (mL) of water according to Schedule B (continuous intake for 14 days followed by one week off treatment in cycles of 21 days).

The Data Monitoring Committee decided on 28 November 2018 to lower the 2.5 mg BI 894999 dose due to safety concerns to 2mg, therefore patients treated before the decision were administered 2.5mg, and patients treated after the decision were administered 2mg.

|  |                    |
|--|--------------------|
| Arm type                               | Experimental       |
| Investigational medicinal product name | BI 894999          |
| Investigational medicinal product code |                    |
| Other name                             |                    |
| Pharmaceutical forms                   | Film-coated tablet |
| Routes of administration               | Oral use           |

**Dosage and administration details:**

Some of the patients of this arm were administered orally 2 milligram (mg) of BI 894999. The rest of the patients in this arm were administered 2.5 mg of BI 894999. BI 894999 administration was performed in the morning, after an overnight fast, 1 hour before breakfast with at least 250 milliliter (mL) of water according to Schedule B (continuous intake for 14 days followed by one week off treatment in cycles of 21 days).

|                  |  |
|------------------|--|
| <b>Arm title</b> | Phase Ib - Schedule B: 2.5 mg BI 894999 (CRC patients) |
|------------------|--|

**Arm description:**

Adult patients diagnosed with colorectal cancer (CRC) were administered orally 2.5 milligram (mg) of BI 894999. BI 894999 administration was performed in the morning, after an overnight fast, 1 hour before breakfast with at least 250 milliliter (mL) of water according to Schedule B (continuous intake for 14 days followed by one week off treatment in cycles of 21 days).

|  |                    |
|--|--------------------|
| Arm type                               | Experimental       |
| Investigational medicinal product name | BI 894999          |
| Investigational medicinal product code |                    |
| Other name                             |                    |
| Pharmaceutical forms                   | Film-coated tablet |
| Routes of administration               | Oral use           |

**Dosage and administration details:**

Patients were administered orally 2.5 milligram (mg) of BI 894999. BI 894999 administration was performed in the morning, after an overnight fast, 1 hour before breakfast with at least 250 milliliter (mL) of water according to Schedule B (continuous intake for 14 days followed by one week off treatment in cycles of 21 days).

|                  |   |
|------------------|---|
| <b>Arm title</b> | Phase Ib - Schedule B: 2 or 2.5 mg BI 894999 (mCRPC patients) |
|------------------|---|

**Arm description:**

This arm included adult patients diagnosed with metastatic castrate resistant prostate cancer (mCRPC).

MCRPC patients were initially administered 2.5 mg of BI 894999. BI 894999 administration was performed in the morning, after an overnight fast, 1 hour before breakfast with at least 250 milliliter (mL) of water according to Schedule B (continuous intake for 14 days followed by one week off treatment in cycles of 21 days).

The Data Monitoring Committee decided on 28 November 2018 to lower the 2.5 mg BI 894999 dose due

to safety concerns to 2mg, therefore patients treated before the decision were administered 2.5mg, and patients treated after the decision were administered 2mg.

|  |                    |
|--|--------------------|
| Arm type                               | Experimental       |
| Investigational medicinal product name | BI 894999          |
| Investigational medicinal product code |                    |
| Other name                             |                    |
| Pharmaceutical forms                   | Film-coated tablet |
| Routes of administration               | Oral use           |

**Dosage and administration details:**

Some of the patients of this arm were administered orally 2 milligram (mg) of BI 894999 once daily. The rest of the patients in this arm were administered orally 2.5 mg of BI 894999. BI 894999 administration was performed in the morning, after an overnight fast, 1 hour before breakfast with at least 250 milliliter (mL) of water according to Schedule B (continuous intake for 14 days followed by one week off treatment in cycles of 21 days).

|                  |   |
|------------------|---|
| <b>Arm title</b> | Phase Ib - Schedule B: 2.5 mg BI 894999 (NC patients) |
|------------------|---|

**Arm description:**

Adult patients diagnosed with NUT carcinoma (NC) were administered orally 2.5 milligram (mg) of BI 894999 once daily, in the morning, after an overnight fast, 1 hour before breakfast with at least 250 milliliter (mL) of water. Schedule B was a continuous intake for 14 days followed by one week off treatment in cycles of 21 days. The 2.5 mg dose could be reduced to 2 mg in case of adverse events.

|  |                    |
|--|--------------------|
| Arm type                               | Experimental       |
| Investigational medicinal product name | BI 894999          |
| Investigational medicinal product code |                    |
| Other name                             |                    |
| Pharmaceutical forms                   | Film-coated tablet |
| Routes of administration               | Oral use           |

**Dosage and administration details:**

Patients were administered orally 2.5 milligram (mg) of BI 894999 once daily, in the morning, after an overnight fast, 1 hour before breakfast with at least 250 milliliter (mL) of water. Schedule B was a continuous intake for 14 days followed by one week off treatment in cycles of 21 days. The 2.5 mg dose could be reduced to 2 mg in case of adverse events.

|                  |  |
|------------------|--|
| <b>Arm title</b> | Phase Ib - Schedule C: 6/3 or 7/3.5 mg BI 894999 (NC patients) |
|------------------|--|

**Arm description:**

This arm included adult patients diagnosed with NUT carcinoma (NC).

The DMC reclaimed the maximum tolerated dose (MTD) as 6/3mg on 08 July 2020 after 1 patient was already treated with 7/3.5mg, so the first patient in NC and all the following patients were treated with 6/3mg.

Patients in were administered orally once daily on Day 1 and on Day 15 of each cycle a loading dose of 6 milligram (mg) of BI 894999, followed by six days intake of the maintenance dose of 3 mg of BI 894999 once daily, followed by one week off, repeated every two weeks in cycles of 28 days (Schedule C).

|  |                    |
|--|--------------------|
| Arm type                               | Experimental       |
| Investigational medicinal product name | BI 894999          |
| Investigational medicinal product code |                    |
| Other name                             |                    |
| Pharmaceutical forms                   | Film-coated tablet |
| Routes of administration               | Oral use           |

**Dosage and administration details:**

Some of the patients in this arm were administered orally once daily on Day 1 and on Day 15 of each cycle a loading dose of 6 milligram (mg) of BI 894999, followed by six days intake of the maintenance dose of 3 mg of BI 894999 once daily, followed by one week off, repeated every two weeks in cycles of 28 days (Schedule C). The rest of the patients in this arm were administered orally once daily on Day 1 of each cycle a loading dose of 7 mg of BI 894999, followed by six days intake of the maintenance dose of 3.5 mg of BI 894999 once daily according to Schedule C.

| <b>Number of subjects in period 1<sup>[1]</sup></b> | Phase Ia - Schedule A: 0.2 mg BI 894999 | Phase Ia - Schedule A: 0.5 mg BI 894999 | Phase Ia - Schedule A: 1 mg BI 894999 |
|---|---|---|---------------------------------------|
| Started   | 2                                       | 2                                       | 3                                     |
| Completed   | 0                                       | 0                                       | 0                                     |
| Not completed                                       | 2                                       | 2                                       | 3                                     |
| Dose limiting toxicity (DLTs)                       | -                                       | -                                       | -                                     |
| Other Adverse Events                                | -                                       | -                                       | -                                     |
| other reasons than listed                           | -                                       | -                                       | -                                     |
| Progressive disease                                 | 2                                       | 2                                       | 3                                     |
| Refused to continue trial medication                | -                                       | -                                       | -                                     |

| <b>Number of subjects in period 1<sup>[1]</sup></b> | Phase Ia - Schedule A: 1.5 mg BI 894999 | Phase Ia - Schedule A: 2 mg BI 894999 | Phase Ia - Schedule A: 5 mg BI 894999 |
|---|---|---------------------------------------|---------------------------------------|
| Started   | 6                                       | 6                                     | 2                                     |
| Completed   | 0                                       | 0                                     | 0                                     |
| Not completed                                       | 6                                       | 6                                     | 2                                     |
| Dose limiting toxicity (DLTs)                       | -                                       | 3                                     | 1                                     |
| Other Adverse Events                                | 1                                       | -                                     | 1                                     |
| other reasons than listed                           | -                                       | -                                     | -                                     |
| Progressive disease                                 | 5                                       | 3                                     | -                                     |
| Refused to continue trial medication                | -                                       | -                                     | -                                     |

| <b>Number of subjects in period 1<sup>[1]</sup></b> | Phase Ia - Schedule B: 1.5 mg BI 894999 | Phase Ia - Schedule B: 2 mg BI 894999 | Phase Ia - Schedule B: 2.5 mg BI 894999 |
|---|---|---------------------------------------|---|
| Started   | 6                                       | 6                                     | 13                                      |
| Completed   | 0                                       | 0                                     | 0                                       |
| Not completed                                       | 6                                       | 6                                     | 13                                      |
| Dose limiting toxicity (DLTs)                       | 1                                       | -                                     | 1                                       |
| Other Adverse Events                                | -                                       | -                                     | -                                       |
| other reasons than listed                           | -                                       | 1                                     | 1                                       |
| Progressive disease                                 | 5                                       | 5                                     | 11                                      |
| Refused to continue trial medication                | -                                       | -                                     | -                                       |

| <b>Number of subjects in period 1<sup>[1]</sup></b> | Phase Ia - Schedule C: 5/2.5 mg BI 894999 | Phase Ia - Schedule C: 6/3 mg BI 894999 | Phase Ia - Schedule C: 7/3.5 mg BI 894999 |
|---|---|---|---|
| Started   | 4   | 15                                      | 12  |
| Completed   | 0   | 0                                       | 0   |
| Not completed                                       | 4   | 15                                      | 12  |
| Dose limiting toxicity (DLTs)                       | -   | -                                       | 1   |
| Other Adverse Events                                | 1   | 3                                       | 2   |
| other reasons than listed                           | -   | 1                                       | 1   |
| Progressive disease                                 | 3   | 10                                      | 8   |
| Refused to continue trial medication                | -   | 1                                       | -   |

| <b>Number of subjects in period 1<sup>[1]</sup></b> | Phase Ia - Schedule B: 1.5 mg BI 894999 (DLBCL patients) | Phase Ia - Schedule B: 2 mg BI 894999 (DLBCL patients) | Phase Ia - Schedule B: 2.5 mg BI 894999 (DLBCL patients) |
|---|--|--|--|
| Started   | 8  | 4  | 2  |
| Completed   | 0  | 0  | 0  |
| Not completed                                       | 8  | 4  | 2  |
| Dose limiting toxicity (DLTs)                       | -  | 1  | -  |
| Other Adverse Events                                | -  | 1  | -  |
| other reasons than listed                           | -  | -  | -  |
| Progressive disease                                 | 8  | 2  | 2  |
| Refused to continue trial medication                | -  | -  | -  |

| <b>Number of subjects in period 1<sup>[1]</sup></b> | Phase Ia - Schedule C: 4/2 mg BI 894999 (DLBCL patients) | Phase Ia - Schedule C: BI 894999 5/2.5 mg (DLBCL patients) | Phase Ib - Schedule B: 2 or 2.5 mg BI 894999 (SCLC patients) |
|---|--|--|--|
| Started   | 2  | 2  | 12   |
| Completed   | 0  | 0  | 0  |
| Not completed                                       | 2  | 2  | 12   |
| Dose limiting toxicity (DLTs)                       | -  | 1  | 1  |
| Other Adverse Events                                | -  | -  | 2  |
| other reasons than listed                           | -  | -  | -  |
| Progressive disease                                 | 2  | 1  | 9  |
| Refused to continue trial medication                | -  | -  | -  |

| <b>Number of subjects in period 1<sup>[1]</sup></b> | Phase Ib - Schedule B: 2.5 mg BI 894999 (CRC patients) | Phase Ib - Schedule B: 2 or 2.5 mg BI 894999 (mCRPC patients) | Phase Ib - Schedule B: 2.5 mg BI 894999 (NC patients) |
|---|--|---|---|
| Started   | 14   | 11  | 20  |
| Completed   | 0  | 0   | 0   |
| Not completed                                       | 14   | 11  | 20  |
| Dose limiting toxicity (DLTs)                       | -  | 2   | -   |
| Other Adverse Events                                | 1  | 2   | 2   |
| other reasons than listed                           | -  | -   | 2   |
| Progressive disease                                 | 12   | 7   | 16  |
| Refused to continue trial medication                | 1  | -   | -   |

| <b>Number of subjects in period 1<sup>[1]</sup></b> | Phase Ib - Schedule C: 6/3 or 7/3.5 mg BI 894999 (NC patients) |
|---|--|
| Started   | 22   |
| Completed   | 0  |
| Not completed                                       | 22   |
| Dose limiting toxicity (DLTs)                       | -  |
| Other Adverse Events                                | 1  |
| other reasons than listed                           | 2  |

|                                      |    |
|--------------------------------------|----|
| Progressive disease                  | 18 |
| Refused to continue trial medication | 1  |

---

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: Out of 231 enrolled patients only 174 entered the trial.

## Baseline characteristics

### Reporting groups

|  |   |
|--|---|
| Reporting group title  | Phase Ia - Schedule A: 0.2 mg BI 894999 |
| Reporting group description:<br>Adult patients with a confirmed diagnosis of advanced, unresectable and/or metastatic malignant solid tumours who had failed conventional treatment or for whom no therapy of proven efficacy existed or who were not amenable to standard therapies were administered orally 0.2 milligram (mg) of BI 894999 once daily, in the morning, after an overnight fast, 1 hour before breakfast with at least 250 milliliter (mL) of water. Schedule A was a continuous daily intake in cycles of 21 days.  |   |
| Reporting group title  | Phase Ia - Schedule A: 0.5 mg BI 894999 |
| Reporting group description:<br>Adult patients with a confirmed diagnosis of advanced, unresectable and/or metastatic malignant solid tumours who had failed conventional treatment or for whom no therapy of proven efficacy existed or who were not amenable to standard therapies were administered orally 0.5 milligram (mg) of BI 894999 once daily, in the morning, after an overnight fast, 1 hour before breakfast with at least 250 milliliter (mL) of water. Schedule A was a continuous daily intake in cycles of 21 days.  |   |
| Reporting group title  | Phase Ia - Schedule A: 1 mg BI 894999   |
| Reporting group description:<br>Adult patients with a confirmed diagnosis of advanced, unresectable and/or metastatic malignant solid tumours who had failed conventional treatment or for whom no therapy of proven efficacy existed or who were not amenable to standard therapies were administered orally 1 milligram (mg) of BI 894999 once daily, in the morning, after an overnight fast, 1 hour before breakfast with at least 250 milliliter (mL) of water. Schedule A was a continuous daily intake in cycles of 21 days.  |   |
| Reporting group title  | Phase Ia - Schedule A: 1.5 mg BI 894999 |
| Reporting group description:<br>Adult patients with a confirmed diagnosis of advanced, unresectable and/or metastatic malignant solid tumours who had failed conventional treatment or for whom no therapy of proven efficacy existed or who were not amenable to standard therapies were administered orally 1.5 milligram (mg) of BI 894999 once daily, in the morning, after an overnight fast, 1 hour before breakfast with at least 250 milliliter (mL) of water. Schedule A was a continuous daily intake in cycles of 21 days.  |   |
| Reporting group title  | Phase Ia - Schedule A: 2 mg BI 894999   |
| Reporting group description:<br>Adult patients with a confirmed diagnosis of advanced, unresectable and/or metastatic malignant solid tumours who had failed conventional treatment or for whom no therapy of proven efficacy existed or who were not amenable to standard therapies were administered orally 2 milligram (mg) of BI 894999 once daily, in the morning, after an overnight fast, 1 hour before breakfast with at least 250 milliliter (mL) of water. Schedule A was a continuous daily intake in cycles of 21 days.  |   |
| Reporting group title  | Phase Ia - Schedule A: 5 mg BI 894999   |
| Reporting group description:<br>Adult patients with a confirmed diagnosis of advanced, unresectable and/or metastatic malignant solid tumours who had failed conventional treatment or for whom no therapy of proven efficacy existed or who were not amenable to standard therapies were administered orally 5 milligram (mg) of BI 894999 once daily, in the morning, after an overnight fast, 1 hour before breakfast with at least 250 milliliter (mL) of water. Schedule A was a continuous daily intake in cycles of 21 days.  |   |
| Reporting group title  | Phase Ia - Schedule B: 1.5 mg BI 894999 |
| Reporting group description:<br>Adult patients with a confirmed diagnosis of advanced, unresectable and/or metastatic malignant solid tumours who had failed conventional treatment or for whom no therapy of proven efficacy existed or who were not amenable to standard therapies were administered orally 1.5 milligram (mg) of BI 894999 once daily, in the morning, after an overnight fast, 1 hour before breakfast with at least 250 milliliter (mL) of water. Schedule B was a continuous intake for 14 days followed by one week off treatment in cycles of 21 days. |   |
| Reporting group title  | Phase Ia - Schedule B: 2 mg BI 894999   |
| Reporting group description:<br>Adult patients with a confirmed diagnosis of advanced, unresectable and/or metastatic malignant solid tumours who had failed conventional treatment or for whom no therapy of proven efficacy existed or who were not amenable to standard therapies were administered orally 2 milligram (mg) of BI 894999 once daily, in the morning, after an overnight fast, 1 hour before breakfast with at least 250 milliliter (mL) of water. Schedule B was a continuous intake for 14 days followed by one week off treatment in                      |   |

cycles of 21 days.

|                       |   |
|-----------------------|---|
| Reporting group title | Phase Ia - Schedule B: 2.5 mg BI 894999 |
|-----------------------|---|

Reporting group description:

Adult patients with a confirmed diagnosis of advanced, unresectable and/or metastatic malignant solid tumours who had failed conventional treatment or for whom no therapy of proven efficacy existed or who were not amenable to standard therapies were administered orally 2.5 mg of BI 894999 once daily, in the morning, after an overnight fast, 1 hour before breakfast with at least 250 milliliter (mL) of water. Schedule B was a continuous intake for 14 days followed by one week off treatment in cycles of 21 days.

|                       |   |
|-----------------------|---|
| Reporting group title | Phase Ia - Schedule C: 5/2.5 mg BI 894999 |
|-----------------------|---|

Reporting group description:

Adult patients with a confirmed diagnosis of advanced, unresectable and/or metastatic malignant solid tumours who had failed conventional treatment or for whom no therapy of proven efficacy existed or who were not amenable to standard therapies were administered orally once daily on Day 1 and on Day 15 of each cycle a loading dose of 5 milligram (mg) of BI 894999, followed by six days daily intake of the maintenance dose of 2.5 mg of BI 894999 once daily, followed by one week off, repeated every two weeks in cycles of 28 days (Schedule C). The loading and the maintenance dose were administered in the morning, after an overnight fast, 1 hour before breakfast with at least 250 milliliter (mL) of water.

|                       |   |
|-----------------------|---|
| Reporting group title | Phase Ia - Schedule C: 6/3 mg BI 894999 |
|-----------------------|---|

Reporting group description:

Adult patients with a confirmed diagnosis of advanced, unresectable and/or metastatic malignant solid tumours who had failed conventional treatment or for whom no therapy of proven efficacy existed or who were not amenable to standard therapies were administered orally once daily on Day 1 and on Day 15 of each cycle a loading dose of 6 milligram (mg) of BI 894999, followed by six days daily intake of the maintenance dose of 3 mg of BI 894999 once daily, followed by one week off, repeated every two weeks in cycles of 28 days (Schedule C). The loading and the maintenance dose were administered in the morning, after an overnight fast, 1 hour before breakfast with at least 250 milliliter (mL) of water.

|                       |   |
|-----------------------|---|
| Reporting group title | Phase Ia - Schedule C: 7/3.5 mg BI 894999 |
|-----------------------|---|

Reporting group description:

Adult patients with a confirmed diagnosis of advanced, unresectable and/or metastatic malignant solid tumours who had failed conventional treatment or for whom no therapy of proven efficacy existed or who were not amenable to standard therapies were administered orally once daily on Day 1 and on Day 15 of each cycle a loading dose of 7 milligram (mg) of BI 894999, followed by six days daily intake of the maintenance dose of 3.5 mg of BI 894999 once daily, followed by one week off, repeated every two weeks in cycles of 28 days (Schedule C). The loading and the maintenance dose were administered in the morning, after an overnight fast, 1 hour before breakfast with at least 250 milliliter (mL) of water.

|                       |  |
|-----------------------|--|
| Reporting group title | Phase Ia - Schedule B: 1.5 mg BI 894999 (DLBCL patients) |
|-----------------------|--|

Reporting group description:

Adult patients with histologically confirmed diagnosis of diffuse large B-cell lymphoma (DLBCL) were administered orally 1.5 milligram (mg) of BI 894999 once daily, in the morning, after an overnight fast, 1 hour before breakfast with at least 250 milliliter (mL) of water. Schedule B was a continuous intake for 14 days followed by one week off treatment in cycles of 21 days.

|                       |  |
|-----------------------|--|
| Reporting group title | Phase Ia - Schedule B: 2 mg BI 894999 (DLBCL patients) |
|-----------------------|--|

Reporting group description:

Adult patients with histologically confirmed diagnosis of diffuse large B-cell lymphoma (DLBCL) were administered orally 2 milligram (mg) of BI 894999 once daily, in the morning, after an overnight fast, 1 hour before breakfast with at least 250 milliliter (mL) of water. Schedule B was a continuous intake for 14 days followed by one week off treatment in cycles of 21 days.

|                       |  |
|-----------------------|--|
| Reporting group title | Phase Ia - Schedule B: 2.5 mg BI 894999 (DLBCL patients) |
|-----------------------|--|

Reporting group description:

Adult patients with histologically confirmed diagnosis of diffuse large B-cell lymphoma (DLBCL) were administered orally 2.5 milligram (mg) of BI 894999 once daily, in the morning, after an overnight fast, 1 hour before breakfast with at least 250 milliliter (mL) of water. Schedule B was a continuous intake for 14 days followed by one week off treatment in cycles of 21 days.

|                       |  |
|-----------------------|--|
| Reporting group title | Phase Ia - Schedule C: 4/2 mg BI 894999 (DLBCL patients) |
|-----------------------|--|

Reporting group description:

Adult patients with histologically confirmed diagnosis of diffuse large B-cell lymphoma (DLBCL) were administered orally once daily on Day 1 and on Day 15 of each cycle a loading dose of 4 milligram (mg) of BI 894999, followed by six days daily intake of the maintenance dose of 2 mg of BI 894999 once daily, followed by one week off, repeated every two weeks in cycles of 28 days (Schedule C). The loading and the maintenance dose were administered in the morning, after an overnight fast, 1 hour before breakfast with at least 250 milliliter (mL) of water.

|                       |  |
|-----------------------|--|
| Reporting group title | Phase Ia - Schedule C: BI 894999 5/2.5 mg (DLBCL patients) |
|-----------------------|--|



Reporting group description:

Adult patients with histologically confirmed diagnosis of diffuse large B-cell lymphoma (DLBCL) were administered orally once daily on Day 1 and on Day 15 of each cycle a loading dose of 5 milligram (mg) of BI 894999, followed by six days daily intake of the maintenance dose of 2.5 mg of BI 894999, followed by one week off, repeated every two weeks in cycles of 28 days (Schedule C). The loading and the maintenance dose were administered in the morning, after an overnight fast, 1 hour before breakfast with at least 250 milliliter (mL) of water.

|                       |  |
|-----------------------|--|
| Reporting group title | Phase Ib - Schedule B: 2 or 2.5 mg BI 894999 (SCLC patients) |
|-----------------------|--|

Reporting group description:

This arm included adult patients diagnosed with small cell lung cancer (SCLC).

SCLC patients were initially administered 2.5 mg of BI 894999. BI 894999 administration was performed in the morning, after an overnight fast, 1 hour before breakfast with at least 250 milliliter (mL) of water according to Schedule B (continuous intake for 14 days followed by one week off treatment in cycles of 21 days).

The Data Monitoring Committee decided on 28 November 2018 to lower the 2.5 mg BI 894999 dose due to safety concerns to 2mg, therefore patients treated before the decision were administered 2.5mg, and patients treated after the decision were administered 2mg.

|                       |  |
|-----------------------|--|
| Reporting group title | Phase Ib - Schedule B: 2.5 mg BI 894999 (CRC patients) |
|-----------------------|--|

Reporting group description:

Adult patients diagnosed with colorectal cancer (CRC) were administered orally 2.5 milligram (mg) of BI 894999. BI 894999 administration was performed in the morning, after an overnight fast, 1 hour before breakfast with at least 250 milliliter (mL) of water according to Schedule B (continuous intake for 14 days followed by one week off treatment in cycles of 21 days).

|                       |   |
|-----------------------|---|
| Reporting group title | Phase Ib - Schedule B: 2 or 2.5 mg BI 894999 (mCRPC patients) |
|-----------------------|---|

Reporting group description:

This arm included adult patients diagnosed with metastatic castrate resistant prostate cancer (mCRPC). MCRPC patients were initially administered 2.5 mg of BI 894999. BI 894999 administration was performed in the morning, after an overnight fast, 1 hour before breakfast with at least 250 milliliter (mL) of water according to Schedule B (continuous intake for 14 days followed by one week off treatment in cycles of 21 days).

The Data Monitoring Committee decided on 28 November 2018 to lower the 2.5 mg BI 894999 dose due to safety concerns to 2mg, therefore patients treated before the decision were administered 2.5mg, and patients treated after the decision were administered 2mg.

|                       |   |
|-----------------------|---|
| Reporting group title | Phase Ib - Schedule B: 2.5 mg BI 894999 (NC patients) |
|-----------------------|---|

Reporting group description:

Adult patients diagnosed with NUT carcinoma (NC) were administered orally 2.5 milligram (mg) of BI 894999 once daily, in the morning, after an overnight fast, 1 hour before breakfast with at least 250 milliliter (mL) of water. Schedule B was a continuous intake for 14 days followed by one week off treatment in cycles of 21 days. The 2.5 mg dose could be reduced to 2 mg in case of adverse events.

|                       |  |
|-----------------------|--|
| Reporting group title | Phase Ib - Schedule C: 6/3 or 7/3.5 mg BI 894999 (NC patients) |
|-----------------------|--|

Reporting group description:

This arm included adult patients diagnosed with NUT carcinoma (NC).

The DMC reclaimed the maximum tolerated dose (MTD) as 6/3mg on 08 July 2020 after 1 patient was already treated with 7/3.5mg, so the first patient in NC and all the following patients were treated with 6/3mg.

Patients in were administered orally once daily on Day 1 and on Day 15 of each cycle a loading dose of 6 milligram (mg) of BI 894999, followed by six days intake of the maintenance dose of 3 mg of BI 894999 once daily, followed by one week off, repeated every two weeks in cycles of 28 days (Schedule C).

| Reporting group values   | Phase Ia - Schedule A: 0.2 mg BI 894999 | Phase Ia - Schedule A: 0.5 mg BI 894999 | Phase Ia - Schedule A: 1 mg BI 894999 |
|--|---|---|---------------------------------------|
| Number of subjects   | 2                                       | 2                                       | 3                                     |
| Age categorical  |   |   |                                       |
| Treated Set (TS): Included all patients who were dispensed study treatment and were documented to have taken at least one dose of the study treatment.<br>For Phase Ib-Schedule B SCLC, Phase Ib-Schedule B mCRPC, DMC lowered the dose of SCLC and mCRPC, thus patients treated prior the decision took 2.5mg BI 894999 and patients treated after the decision received 2mg. For Phase Ib - Schedule C NC, the dose was lowered since DMC reclaimed the MTD as 6/3mg after 1 patient already treated with 7/3.5mg. |   |   |                                       |

|  |        |       |       |
|--|--------|-------|-------|
| Units: Subjects  |        |       |       |
| In utero   | 0      | 0     | 0     |
| Preterm newborn infants<br>(gestational age < 37 wks)  | 0      | 0     | 0     |
| Newborns (0-27 days)   | 0      | 0     | 0     |
| Infants and toddlers (28 days-23<br>months)  | 0      | 0     | 0     |
| Children (2-11 years)  | 0      | 0     | 0     |
| Adolescents (12-17 years)  | 0      | 0     | 0     |
| Adults (18-64 years)   | 1      | 0     | 3     |
| From 65-84 years   | 1      | 2     | 0     |
| 85 years and over  | 0      | 0     | 0     |
| Age Continuous   |        |       |       |
| <p>Treated Set (TS): Included all patients who were dispensed study treatment and were documented to have taken at least one dose of the study treatment.</p> <p>For Phase Ib-Schedule B SCLC, Phase Ib-Schedule B mCRPC, DMC lowered the dose of SCLC and mCRPC, thus patients treated prior the decision took 2.5mg BI 894999 and patients treated after the decision received 2mg . For Phase Ib - Schedule C NC, the dose was lowered since DMC reclaimed the MTD as 6/3mg after 1 patient already treated with 7/3.5mg.</p> |        |       |       |
| Units: years   |        |       |       |
| arithmetic mean  | 63.5   | 69.5  | 46.7  |
| standard deviation   | ± 10.6 | ± 2.1 | ± 9.3 |
| Sex: Female, Male  |        |       |       |
| <p>Treated Set (TS): Included all patients who were dispensed study treatment and were documented to have taken at least one dose of the study treatment.</p> <p>For Phase Ib-Schedule B SCLC, Phase Ib-Schedule B mCRPC, DMC lowered the dose of SCLC and mCRPC, thus patients treated prior the decision took 2.5mg BI 894999 and patients treated after the decision received 2mg. For Phase Ib - Schedule C NC, the dose was lowered since DMC reclaimed the MTD as 6/3mg after 1 patient already treated with 7/3.5mg.</p>  |        |       |       |
| Units: Participants  |        |       |       |
| Female   | 1      | 0     | 2     |
| Male   | 1      | 2     | 1     |
| Race (NIH/OMB)   |        |       |       |
| <p>Treated Set (TS): Included all patients who were dispensed study treatment and were documented to have taken at least one dose of the study treatment.</p> <p>For Phase Ib-Schedule B SCLC, Phase Ib-Schedule B mCRPC, DMC lowered the dose of SCLC and mCRPC, thus patients treated prior the decision took 2.5mg BI 894999 and patients treated after the decision received 2mg. For Phase Ib - Schedule C NC, the dose was lowered since DMC reclaimed the MTD as 6/3mg after 1 patient already treated with 7/3.5mg.</p>  |        |       |       |
| Units: Subjects  |        |       |       |
| American Indian or Alaska Native   | 0      | 0     | 0     |
| Asian  | 0      | 0     | 0     |
| Native Hawaiian or Other Pacific<br>Islander   | 0      | 0     | 0     |
| Black or African American  | 0      | 0     | 0     |
| White  | 2      | 2     | 3     |
| More than one race   | 0      | 0     | 0     |
| Unknown or Not Reported  | 0      | 0     | 0     |
| Ethnicity (NIH/OMB)  |        |       |       |
| <p>Treated Set (TS): Included all patients who were dispensed study treatment and were documented to have taken at least one dose of the study treatment.</p> <p>For Phase Ib-Schedule B SCLC, Phase Ib-Schedule B mCRPC, DMC lowered the dose of SCLC and mCRPC, thus patients treated prior the decision took 2.5mg BI 894999 and patients treated after the decision received 2mg. For Phase Ib - Schedule C NC, the dose was lowered since DMC reclaimed the MTD as 6/3mg after 1 patient already treated with 7/3.5mg.</p>  |        |       |       |
| Units: Subjects  |        |       |       |
| Hispanic or Latino   | 0      | 0     | 0     |
| Not Hispanic or Latino   | 2      | 2     | 3     |

|                         |   |   |   |
|-------------------------|---|---|---|
| Unknown or Not Reported | 0 | 0 | 0 |
|-------------------------|---|---|---|

| Reporting group values  | Phase Ia - Schedule A: 1.5 mg BI 894999 | Phase Ia - Schedule A: 2 mg BI 894999 | Phase Ia - Schedule A: 5 mg BI 894999 |
|---|---|---------------------------------------|---------------------------------------|
| Number of subjects  | 6                                       | 6                                     | 2                                     |
| Age categorical   |   |                                       |                                       |
| Treated Set (TS): Included all patients who were dispensed study treatment and were documented to have taken at least one dose of the study treatment.<br>For Phase Ib-Schedule B SCLC, Phase Ib-Schedule B mCRPC, DMC lowered the dose of SCLC and mCRPC, thus patients treated prior the decision took 2.5mg BI 894999 and patients treated after the decision received 2mg. For Phase Ib - Schedule C NC, the dose was lowered since DMC reclaimed the MTD as 6/3mg after 1 patient already treated with 7/3.5mg.  |   |                                       |                                       |
| Units: Subjects   |   |                                       |                                       |
| In utero  | 0                                       | 0                                     | 0                                     |
| Preterm newborn infants (gestational age < 37 wks)  | 0                                       | 0                                     | 0                                     |
| Newborns (0-27 days)  | 0                                       | 0                                     | 0                                     |
| Infants and toddlers (28 days-23 months)  | 0                                       | 0                                     | 0                                     |
| Children (2-11 years)   | 0                                       | 0                                     | 0                                     |
| Adolescents (12-17 years)   | 0                                       | 0                                     | 0                                     |
| Adults (18-64 years)  | 5                                       | 3                                     | 1                                     |
| From 65-84 years  | 1                                       | 3                                     | 1                                     |
| 85 years and over   | 0                                       | 0                                     | 0                                     |
| Age Continuous  |   |                                       |                                       |
| Treated Set (TS): Included all patients who were dispensed study treatment and were documented to have taken at least one dose of the study treatment.<br>For Phase Ib-Schedule B SCLC, Phase Ib-Schedule B mCRPC, DMC lowered the dose of SCLC and mCRPC, thus patients treated prior the decision took 2.5mg BI 894999 and patients treated after the decision received 2mg . For Phase Ib - Schedule C NC, the dose was lowered since DMC reclaimed the MTD as 6/3mg after 1 patient already treated with 7/3.5mg. |   |                                       |                                       |
| Units: years  |   |                                       |                                       |
| arithmetic mean   | 57.5                                    | 53.5                                  | 54.5                                  |
| standard deviation  | ± 11.9                                  | ± 18.1                                | ± 26.2                                |
| Sex: Female, Male   |   |                                       |                                       |
| Treated Set (TS): Included all patients who were dispensed study treatment and were documented to have taken at least one dose of the study treatment.<br>For Phase Ib-Schedule B SCLC, Phase Ib-Schedule B mCRPC, DMC lowered the dose of SCLC and mCRPC, thus patients treated prior the decision took 2.5mg BI 894999 and patients treated after the decision received 2mg. For Phase Ib - Schedule C NC, the dose was lowered since DMC reclaimed the MTD as 6/3mg after 1 patient already treated with 7/3.5mg.  |   |                                       |                                       |
| Units: Participants   |   |                                       |                                       |
| Female  | 2                                       | 6                                     | 0                                     |
| Male  | 4                                       | 0                                     | 2                                     |
| Race (NIH/OMB)  |   |                                       |                                       |
| Treated Set (TS): Included all patients who were dispensed study treatment and were documented to have taken at least one dose of the study treatment.<br>For Phase Ib-Schedule B SCLC, Phase Ib-Schedule B mCRPC, DMC lowered the dose of SCLC and mCRPC, thus patients treated prior the decision took 2.5mg BI 894999 and patients treated after the decision received 2mg. For Phase Ib - Schedule C NC, the dose was lowered since DMC reclaimed the MTD as 6/3mg after 1 patient already treated with 7/3.5mg.  |   |                                       |                                       |
| Units: Subjects   |   |                                       |                                       |
| American Indian or Alaska Native  | 0                                       | 0                                     | 0                                     |
| Asian   | 0                                       | 0                                     | 0                                     |
| Native Hawaiian or Other Pacific Islander   | 0                                       | 0                                     | 0                                     |

|  |   |   |   |
|--|---|---|---|
| Black or African American  | 0 | 0 | 0 |
| White  | 6 | 6 | 2 |
| More than one race   | 0 | 0 | 0 |
| Unknown or Not Reported  | 0 | 0 | 0 |
| Ethnicity (NIH/OMB)  |   |   |   |
| Treated Set (TS): Included all patients who were dispensed study treatment and were documented to have taken at least one dose of the study treatment.<br>For Phase Ib-Schedule B SCLC, Phase Ib-Schedule B mCRPC, DMC lowered the dose of SCLC and mCRPC, thus patients treated prior the decision took 2.5mg BI 894999 and patients treated after the decision received 2mg. For Phase Ib - Schedule C NC, the dose was lowered since DMC reclaimed the MTD as 6/3mg after 1 patient already treated with 7/3.5mg. |   |   |   |
| Units: Subjects  |   |   |   |
| Hispanic or Latino   | 0 | 1 | 0 |
| Not Hispanic or Latino   | 6 | 5 | 2 |
| Unknown or Not Reported  | 0 | 0 | 0 |

| Reporting group values  | Phase Ia - Schedule B: 1.5 mg BI 894999 | Phase Ia - Schedule B: 2 mg BI 894999 | Phase Ia - Schedule B: 2.5 mg BI 894999 |
|---|---|---------------------------------------|---|
| Number of subjects  | 6                                       | 6                                     | 13                                      |
| Age categorical   |   |                                       |   |
| Treated Set (TS): Included all patients who were dispensed study treatment and were documented to have taken at least one dose of the study treatment.<br>For Phase Ib-Schedule B SCLC, Phase Ib-Schedule B mCRPC, DMC lowered the dose of SCLC and mCRPC, thus patients treated prior the decision took 2.5mg BI 894999 and patients treated after the decision received 2mg. For Phase Ib - Schedule C NC, the dose was lowered since DMC reclaimed the MTD as 6/3mg after 1 patient already treated with 7/3.5mg.  |   |                                       |   |
| Units: Subjects   |   |                                       |   |
| In utero  | 0                                       | 0                                     | 0                                       |
| Preterm newborn infants (gestational age < 37 wks)  | 0                                       | 0                                     | 0                                       |
| Newborns (0-27 days)  | 0                                       | 0                                     | 0                                       |
| Infants and toddlers (28 days-23 months)  | 0                                       | 0                                     | 0                                       |
| Children (2-11 years)   | 0                                       | 0                                     | 0                                       |
| Adolescents (12-17 years)   | 0                                       | 0                                     | 0                                       |
| Adults (18-64 years)  | 4                                       | 4                                     | 7                                       |
| From 65-84 years  | 2                                       | 2                                     | 6                                       |
| 85 years and over   | 0                                       | 0                                     | 0                                       |
| Age Continuous  |   |                                       |   |
| Treated Set (TS): Included all patients who were dispensed study treatment and were documented to have taken at least one dose of the study treatment.<br>For Phase Ib-Schedule B SCLC, Phase Ib-Schedule B mCRPC, DMC lowered the dose of SCLC and mCRPC, thus patients treated prior the decision took 2.5mg BI 894999 and patients treated after the decision received 2mg . For Phase Ib - Schedule C NC, the dose was lowered since DMC reclaimed the MTD as 6/3mg after 1 patient already treated with 7/3.5mg. |   |                                       |   |
| Units: years  |   |                                       |   |
| arithmetic mean   | 60.7                                    | 61.5                                  | 64.5                                    |
| standard deviation  | ± 10.8                                  | ± 13.0                                | ± 7.5                                   |
| Sex: Female, Male   |   |                                       |   |
| Treated Set (TS): Included all patients who were dispensed study treatment and were documented to have taken at least one dose of the study treatment.<br>For Phase Ib-Schedule B SCLC, Phase Ib-Schedule B mCRPC, DMC lowered the dose of SCLC and mCRPC, thus patients treated prior the decision took 2.5mg BI 894999 and patients treated after the decision received 2mg. For Phase Ib - Schedule C NC, the dose was lowered since DMC reclaimed the MTD as 6/3mg after 1 patient already treated with 7/3.5mg.  |   |                                       |   |
| Units: Participants   |   |                                       |   |
| Female  | 3                                       | 1                                     | 4                                       |
| Male  | 3                                       | 5                                     | 9                                       |

|   |   |   |    |
|---|---|---|----|
| Race (NIH/OMB)  |   |   |    |
| <p>Treated Set (TS): Included all patients who were dispensed study treatment and were documented to have taken at least one dose of the study treatment.</p> <p>For Phase Ib-Schedule B SCLC, Phase Ib-Schedule B mCRPC, DMC lowered the dose of SCLC and mCRPC, thus patients treated prior the decision took 2.5mg BI 894999 and patients treated after the decision received 2mg. For Phase Ib - Schedule C NC, the dose was lowered since DMC reclaimed the MTD as 6/3mg after 1 patient already treated with 7/3.5mg.</p> |   |   |    |
| Units: Subjects   |   |   |    |
| American Indian or Alaska Native  | 0 | 0 | 0  |
| Asian   | 0 | 0 | 0  |
| Native Hawaiian or Other Pacific Islander   | 0 | 0 | 0  |
| Black or African American   | 0 | 0 | 0  |
| White   | 6 | 6 | 13 |
| More than one race  | 0 | 0 | 0  |
| Unknown or Not Reported   | 0 | 0 | 0  |
| Ethnicity (NIH/OMB)   |   |   |    |
| <p>Treated Set (TS): Included all patients who were dispensed study treatment and were documented to have taken at least one dose of the study treatment.</p> <p>For Phase Ib-Schedule B SCLC, Phase Ib-Schedule B mCRPC, DMC lowered the dose of SCLC and mCRPC, thus patients treated prior the decision took 2.5mg BI 894999 and patients treated after the decision received 2mg. For Phase Ib - Schedule C NC, the dose was lowered since DMC reclaimed the MTD as 6/3mg after 1 patient already treated with 7/3.5mg.</p> |   |   |    |
| Units: Subjects   |   |   |    |
| Hispanic or Latino  | 0 | 0 | 0  |
| Not Hispanic or Latino  | 6 | 6 | 13 |
| Unknown or Not Reported   | 0 | 0 | 0  |

| Reporting group values   | Phase Ia - Schedule C: 5/2.5 mg BI 894999 | Phase Ia - Schedule C: 6/3 mg BI 894999 | Phase Ia - Schedule C: 7/3.5 mg BI 894999 |
|--|---|---|---|
| Number of subjects   | 4   | 15                                      | 12  |
| Age categorical  |   |   |   |
| <p>Treated Set (TS): Included all patients who were dispensed study treatment and were documented to have taken at least one dose of the study treatment.</p> <p>For Phase Ib-Schedule B SCLC, Phase Ib-Schedule B mCRPC, DMC lowered the dose of SCLC and mCRPC, thus patients treated prior the decision took 2.5mg BI 894999 and patients treated after the decision received 2mg. For Phase Ib - Schedule C NC, the dose was lowered since DMC reclaimed the MTD as 6/3mg after 1 patient already treated with 7/3.5mg.</p>  |   |   |   |
| Units: Subjects  |   |   |   |
| In utero   | 0   | 0                                       | 0   |
| Preterm newborn infants (gestational age < 37 wks)   | 0   | 0                                       | 0   |
| Newborns (0-27 days)   | 0   | 0                                       | 0   |
| Infants and toddlers (28 days-23 months)   | 0   | 0                                       | 0   |
| Children (2-11 years)  | 0   | 0                                       | 0   |
| Adolescents (12-17 years)  | 0   | 0                                       | 0   |
| Adults (18-64 years)   | 2   | 10                                      | 8   |
| From 65-84 years   | 2   | 5                                       | 4   |
| 85 years and over  | 0   | 0                                       | 0   |
| Age Continuous   |   |   |   |
| <p>Treated Set (TS): Included all patients who were dispensed study treatment and were documented to have taken at least one dose of the study treatment.</p> <p>For Phase Ib-Schedule B SCLC, Phase Ib-Schedule B mCRPC, DMC lowered the dose of SCLC and mCRPC, thus patients treated prior the decision took 2.5mg BI 894999 and patients treated after the decision received 2mg . For Phase Ib - Schedule C NC, the dose was lowered since DMC reclaimed the MTD as 6/3mg after 1 patient already treated with 7/3.5mg.</p> |   |   |   |
| Units: years   |   |   |   |

|                    |        |        |       |
|--------------------|--------|--------|-------|
| arithmetic mean    | 63.3   | 59.7   | 62.5  |
| standard deviation | ± 12.8 | ± 12.0 | ± 6.5 |

|  |   |    |    |
|--|---|----|----|
| Sex: Female, Male  |   |    |    |
| Treated Set (TS): Included all patients who were dispensed study treatment and were documented to have taken at least one dose of the study treatment.<br>For Phase Ib-Schedule B SCLC, Phase Ib-Schedule B mCRPC, DMC lowered the dose of SCLC and mCRPC, thus patients treated prior the decision took 2.5mg BI 894999 and patients treated after the decision received 2mg. For Phase Ib - Schedule C NC, the dose was lowered since DMC reclaimed the MTD as 6/3mg after 1 patient already treated with 7/3.5mg. |   |    |    |
| Units: Participants  |   |    |    |
| Female   | 2 | 5  | 7  |
| Male   | 2 | 10 | 5  |
| Race (NIH/OMB)   |   |    |    |
| Treated Set (TS): Included all patients who were dispensed study treatment and were documented to have taken at least one dose of the study treatment.<br>For Phase Ib-Schedule B SCLC, Phase Ib-Schedule B mCRPC, DMC lowered the dose of SCLC and mCRPC, thus patients treated prior the decision took 2.5mg BI 894999 and patients treated after the decision received 2mg. For Phase Ib - Schedule C NC, the dose was lowered since DMC reclaimed the MTD as 6/3mg after 1 patient already treated with 7/3.5mg. |   |    |    |
| Units: Subjects  |   |    |    |
| American Indian or Alaska Native   | 0 | 0  | 0  |
| Asian  | 0 | 0  | 0  |
| Native Hawaiian or Other Pacific Islander  | 0 | 0  | 0  |
| Black or African American  | 0 | 0  | 0  |
| White  | 4 | 15 | 12 |
| More than one race   | 0 | 0  | 0  |
| Unknown or Not Reported  | 0 | 0  | 0  |
| Ethnicity (NIH/OMB)  |   |    |    |
| Treated Set (TS): Included all patients who were dispensed study treatment and were documented to have taken at least one dose of the study treatment.<br>For Phase Ib-Schedule B SCLC, Phase Ib-Schedule B mCRPC, DMC lowered the dose of SCLC and mCRPC, thus patients treated prior the decision took 2.5mg BI 894999 and patients treated after the decision received 2mg. For Phase Ib - Schedule C NC, the dose was lowered since DMC reclaimed the MTD as 6/3mg after 1 patient already treated with 7/3.5mg. |   |    |    |
| Units: Subjects  |   |    |    |
| Hispanic or Latino   | 0 | 1  | 2  |
| Not Hispanic or Latino   | 4 | 14 | 10 |
| Unknown or Not Reported  | 0 | 0  | 0  |

| Reporting group values   | Phase Ia - Schedule B: 1.5 mg BI 894999 (DLBCL patients) | Phase Ia - Schedule B: 2 mg BI 894999 (DLBCL patients) | Phase Ia - Schedule B: 2.5 mg BI 894999 (DLBCL patients) |
|--|--|--|--|
| Number of subjects   | 8  | 4  | 2  |
| Age categorical  |  |  |  |
| Treated Set (TS): Included all patients who were dispensed study treatment and were documented to have taken at least one dose of the study treatment.<br>For Phase Ib-Schedule B SCLC, Phase Ib-Schedule B mCRPC, DMC lowered the dose of SCLC and mCRPC, thus patients treated prior the decision took 2.5mg BI 894999 and patients treated after the decision received 2mg. For Phase Ib - Schedule C NC, the dose was lowered since DMC reclaimed the MTD as 6/3mg after 1 patient already treated with 7/3.5mg. |  |  |  |
| Units: Subjects  |  |  |  |
| In utero   | 0  | 0  | 0  |
| Preterm newborn infants (gestational age < 37 wks)   | 0  | 0  | 0  |
| Newborns (0-27 days)   | 0  | 0  | 0  |

|  |  |  |  |
|--|--|--|--|
| Infants and toddlers (28 days-23 months)   | 0  | 0  | 0  |
| Children (2-11 years)  | 0  | 0  | 0  |
| Adolescents (12-17 years)  | 0  | 0  | 0  |
| Adults (18-64 years)   | 3  | 0  | 0  |
| From 65-84 years   | 5  | 2  | 2  |
| 85 years and over  | 0  | 2  | 0  |
| Age Continuous   |  |  |  |
| <p>Treated Set (TS): Included all patients who were dispensed study treatment and were documented to have taken at least one dose of the study treatment.</p> <p>For Phase Ib-Schedule B SCLC, Phase Ib-Schedule B mCRPC, DMC lowered the dose of SCLC and mCRPC, thus patients treated prior the decision took 2.5mg BI 894999 and patients treated after the decision received 2mg . For Phase Ib - Schedule C NC, the dose was lowered since DMC reclaimed the MTD as 6/3mg after 1 patient already treated with 7/3.5mg.</p> |  |  |  |
| Units: years   |  |  |  |
| arithmetic mean  | 71.4   | 78.8   | 68.5   |
| standard deviation   | ± 10.9   | ± 9.0  | ± 2.1  |
| Sex: Female, Male  |  |  |  |
| <p>Treated Set (TS): Included all patients who were dispensed study treatment and were documented to have taken at least one dose of the study treatment.</p> <p>For Phase Ib-Schedule B SCLC, Phase Ib-Schedule B mCRPC, DMC lowered the dose of SCLC and mCRPC, thus patients treated prior the decision took 2.5mg BI 894999 and patients treated after the decision received 2mg. For Phase Ib - Schedule C NC, the dose was lowered since DMC reclaimed the MTD as 6/3mg after 1 patient already treated with 7/3.5mg.</p>  |  |  |  |
| Units: Participants  |  |  |  |
| Female   | 1  | 1  | 1  |
| Male   | 7  | 3  | 1  |
| Race (NIH/OMB)   |  |  |  |
| <p>Treated Set (TS): Included all patients who were dispensed study treatment and were documented to have taken at least one dose of the study treatment.</p> <p>For Phase Ib-Schedule B SCLC, Phase Ib-Schedule B mCRPC, DMC lowered the dose of SCLC and mCRPC, thus patients treated prior the decision took 2.5mg BI 894999 and patients treated after the decision received 2mg. For Phase Ib - Schedule C NC, the dose was lowered since DMC reclaimed the MTD as 6/3mg after 1 patient already treated with 7/3.5mg.</p>  |  |  |  |
| Units: Subjects  |  |  |  |
| American Indian or Alaska Native   | 0  | 0  | 0  |
| Asian  | 0  | 0  | 0  |
| Native Hawaiian or Other Pacific Islander  | 0  | 0  | 0  |
| Black or African American  | 0  | 0  | 0  |
| White  | 2  | 4  | 2  |
| More than one race   | 0  | 0  | 0  |
| Unknown or Not Reported  | 6  | 0  | 0  |
| Ethnicity (NIH/OMB)  |  |  |  |
| <p>Treated Set (TS): Included all patients who were dispensed study treatment and were documented to have taken at least one dose of the study treatment.</p> <p>For Phase Ib-Schedule B SCLC, Phase Ib-Schedule B mCRPC, DMC lowered the dose of SCLC and mCRPC, thus patients treated prior the decision took 2.5mg BI 894999 and patients treated after the decision received 2mg. For Phase Ib - Schedule C NC, the dose was lowered since DMC reclaimed the MTD as 6/3mg after 1 patient already treated with 7/3.5mg.</p>  |  |  |  |
| Units: Subjects  |  |  |  |
| Hispanic or Latino   | 0  | 0  | 0  |
| Not Hispanic or Latino   | 2  | 4  | 2  |
| Unknown or Not Reported  | 6  | 0  | 0  |
| <b>Reporting group values</b>  | Phase Ia - Schedule C: 4/2 mg BI 894999 (DLBCL patients) | Phase Ia - Schedule C: BI 894999 5/2.5 mg (DLBCL patients) | Phase Ib - Schedule B: 2 or 2.5 mg BI 894999 (SCLC patients) |

|  |       |       |       |
|--|-------|-------|-------|
| Number of subjects   | 2     | 2     | 12    |
| Age categorical  |       |       |       |
| <p>Treated Set (TS): Included all patients who were dispensed study treatment and were documented to have taken at least one dose of the study treatment.</p> <p>For Phase Ib-Schedule B SCLC, Phase Ib-Schedule B mCRPC, DMC lowered the dose of SCLC and mCRPC, thus patients treated prior the decision took 2.5mg BI 894999 and patients treated after the decision received 2mg. For Phase Ib - Schedule C NC, the dose was lowered since DMC reclaimed the MTD as 6/3mg after 1 patient already treated with 7/3.5mg.</p>  |       |       |       |
| Units: Subjects  |       |       |       |
| In utero   | 0     | 0     | 0     |
| Preterm newborn infants (gestational age < 37 wks)   | 0     | 0     | 0     |
| Newborns (0-27 days)   | 0     | 0     | 0     |
| Infants and toddlers (28 days-23 months)   | 0     | 0     | 0     |
| Children (2-11 years)  | 0     | 0     | 0     |
| Adolescents (12-17 years)  | 0     | 0     | 0     |
| Adults (18-64 years)   | 0     | 0     | 7     |
| From 65-84 years   | 2     | 1     | 5     |
| 85 years and over  | 0     | 1     | 0     |
| Age Continuous   |       |       |       |
| <p>Treated Set (TS): Included all patients who were dispensed study treatment and were documented to have taken at least one dose of the study treatment.</p> <p>For Phase Ib-Schedule B SCLC, Phase Ib-Schedule B mCRPC, DMC lowered the dose of SCLC and mCRPC, thus patients treated prior the decision took 2.5mg BI 894999 and patients treated after the decision received 2mg . For Phase Ib - Schedule C NC, the dose was lowered since DMC reclaimed the MTD as 6/3mg after 1 patient already treated with 7/3.5mg.</p> |       |       |       |
| Units: years   |       |       |       |
| arithmetic mean  | 68.5  | 79.0  | 63.5  |
| standard deviation   | ± 2.1 | ± 9.9 | ± 7.3 |
| Sex: Female, Male  |       |       |       |
| <p>Treated Set (TS): Included all patients who were dispensed study treatment and were documented to have taken at least one dose of the study treatment.</p> <p>For Phase Ib-Schedule B SCLC, Phase Ib-Schedule B mCRPC, DMC lowered the dose of SCLC and mCRPC, thus patients treated prior the decision took 2.5mg BI 894999 and patients treated after the decision received 2mg. For Phase Ib - Schedule C NC, the dose was lowered since DMC reclaimed the MTD as 6/3mg after 1 patient already treated with 7/3.5mg.</p>  |       |       |       |
| Units: Participants  |       |       |       |
| Female   | 0     | 1     | 5     |
| Male   | 2     | 1     | 7     |
| Race (NIH/OMB)   |       |       |       |
| <p>Treated Set (TS): Included all patients who were dispensed study treatment and were documented to have taken at least one dose of the study treatment.</p> <p>For Phase Ib-Schedule B SCLC, Phase Ib-Schedule B mCRPC, DMC lowered the dose of SCLC and mCRPC, thus patients treated prior the decision took 2.5mg BI 894999 and patients treated after the decision received 2mg. For Phase Ib - Schedule C NC, the dose was lowered since DMC reclaimed the MTD as 6/3mg after 1 patient already treated with 7/3.5mg.</p>  |       |       |       |
| Units: Subjects  |       |       |       |
| American Indian or Alaska Native   | 0     | 0     | 0     |
| Asian  | 0     | 0     | 0     |
| Native Hawaiian or Other Pacific Islander  | 0     | 0     | 0     |
| Black or African American  | 0     | 0     | 1     |
| White  | 1     | 0     | 7     |
| More than one race   | 0     | 0     | 0     |
| Unknown or Not Reported  | 1     | 2     | 4     |
| Ethnicity (NIH/OMB)  |       |       |       |
| Treated Set (TS): Included all patients who were dispensed study treatment and were documented to  |       |       |       |



|   |   |   |   |
|---|---|---|---|
| <p>have taken at least one dose of the study treatment.</p> <p>For Phase Ib-Schedule B SCLC, Phase Ib-Schedule B mCRPC, DMC lowered the dose of SCLC and mCRPC, thus patients treated prior the decision took 2.5mg BI 894999 and patients treated after the decision received 2mg. For Phase Ib - Schedule C NC, the dose was lowered since DMC reclaimed the MTD as 6/3mg after 1 patient already treated with 7/3.5mg.</p> |   |   |   |
| Units: Subjects   |   |   |   |
| Hispanic or Latino  | 0 | 0 | 0 |
| Not Hispanic or Latino  | 2 | 1 | 8 |
| Unknown or Not Reported   | 0 | 1 | 4 |

| Reporting group values | Phase Ib - Schedule B: 2.5 mg BI 894999 (CRC patients) | Phase Ib - Schedule B: 2 or 2.5 mg BI 894999 (mCRPC patients) | Phase Ib - Schedule B: 2.5 mg BI 894999 (NC patients) |
|------------------------|--|---|---|
| Number of subjects     | 14   | 11  | 20  |
| Age categorical        |  |   |   |

Treated Set (TS): Included all patients who were dispensed study treatment and were documented to have taken at least one dose of the study treatment.

For Phase Ib-Schedule B SCLC, Phase Ib-Schedule B mCRPC, DMC lowered the dose of SCLC and mCRPC, thus patients treated prior the decision took 2.5mg BI 894999 and patients treated after the decision received 2mg. For Phase Ib - Schedule C NC, the dose was lowered since DMC reclaimed the MTD as 6/3mg after 1 patient already treated with 7/3.5mg.

|  |   |   |    |
|--|---|---|----|
| Units: Subjects                                    |   |   |    |
| In utero   | 0 | 0 | 0  |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | 0  |
| Newborns (0-27 days)                               | 0 | 0 | 0  |
| Infants and toddlers (28 days-23 months)           | 0 | 0 | 0  |
| Children (2-11 years)                              | 0 | 0 | 0  |
| Adolescents (12-17 years)                          | 0 | 0 | 0  |
| Adults (18-64 years)                               | 6 | 2 | 18 |
| From 65-84 years                                   | 8 | 9 | 2  |
| 85 years and over                                  | 0 | 0 | 0  |
| Age Continuous                                     |   |   |    |

Treated Set (TS): Included all patients who were dispensed study treatment and were documented to have taken at least one dose of the study treatment.

For Phase Ib-Schedule B SCLC, Phase Ib-Schedule B mCRPC, DMC lowered the dose of SCLC and mCRPC, thus patients treated prior the decision took 2.5mg BI 894999 and patients treated after the decision received 2mg. For Phase Ib - Schedule C NC, the dose was lowered since DMC reclaimed the MTD as 6/3mg after 1 patient already treated with 7/3.5mg.

|                    |       |       |        |
|--------------------|-------|-------|--------|
| Units: years       |       |       |        |
| arithmetic mean    | 66.2  | 69.7  | 44.4   |
| standard deviation | ± 6.3 | ± 4.1 | ± 13.9 |
| Sex: Female, Male  |       |       |        |

Treated Set (TS): Included all patients who were dispensed study treatment and were documented to have taken at least one dose of the study treatment.

For Phase Ib-Schedule B SCLC, Phase Ib-Schedule B mCRPC, DMC lowered the dose of SCLC and mCRPC, thus patients treated prior the decision took 2.5mg BI 894999 and patients treated after the decision received 2mg. For Phase Ib - Schedule C NC, the dose was lowered since DMC reclaimed the MTD as 6/3mg after 1 patient already treated with 7/3.5mg.

|                     |   |    |    |
|---------------------|---|----|----|
| Units: Participants |   |    |    |
| Female              | 6 | 0  | 5  |
| Male                | 8 | 11 | 15 |
| Race (NIH/OMB)      |   |    |    |

Treated Set (TS): Included all patients who were dispensed study treatment and were documented to have taken at least one dose of the study treatment.

For Phase Ib-Schedule B SCLC, Phase Ib-Schedule B mCRPC, DMC lowered the dose of SCLC and mCRPC, thus patients treated prior the decision took 2.5mg BI 894999 and patients treated after the decision received 2mg. For Phase Ib - Schedule C NC, the dose was lowered since DMC reclaimed the

|   |   |   |    |
|---|---|---|----|
| MTD as 6/3mg after 1 patient already treated with 7/3.5mg.  |   |   |    |
| Units: Subjects   |   |   |    |
| American Indian or Alaska Native  | 0 | 0 | 0  |
| Asian   | 0 | 0 | 3  |
| Native Hawaiian or Other Pacific Islander   | 0 | 0 | 0  |
| Black or African American   | 0 | 1 | 0  |
| White   | 9 | 8 | 14 |
| More than one race  | 0 | 0 | 0  |
| Unknown or Not Reported   | 5 | 2 | 3  |
| Ethnicity (NIH/OMB)   |   |   |    |
| <p>Treated Set (TS): Included all patients who were dispensed study treatment and were documented to have taken at least one dose of the study treatment.</p> <p>For Phase Ib-Schedule B SCLC, Phase Ib-Schedule B mCRPC, DMC lowered the dose of SCLC and mCRPC, thus patients treated prior the decision took 2.5mg BI 894999 and patients treated after the decision received 2mg. For Phase Ib - Schedule C NC, the dose was lowered since DMC reclaimed the MTD as 6/3mg after 1 patient already treated with 7/3.5mg.</p> |   |   |    |
| Units: Subjects   |   |   |    |
| Hispanic or Latino  | 1 | 0 | 0  |
| Not Hispanic or Latino  | 8 | 9 | 17 |
| Unknown or Not Reported   | 5 | 2 | 3  |

| Reporting group values  | Phase Ib - Schedule C: 6/3 or 7/3.5 mg BI 894999 (NC patients) | Total |  |
|---|--|-------|--|
| Number of subjects  | 22   | 174   |  |
| Age categorical   |  |       |  |
| <p>Treated Set (TS): Included all patients who were dispensed study treatment and were documented to have taken at least one dose of the study treatment.</p> <p>For Phase Ib-Schedule B SCLC, Phase Ib-Schedule B mCRPC, DMC lowered the dose of SCLC and mCRPC, thus patients treated prior the decision took 2.5mg BI 894999 and patients treated after the decision received 2mg. For Phase Ib - Schedule C NC, the dose was lowered since DMC reclaimed the MTD as 6/3mg after 1 patient already treated with 7/3.5mg.</p> |  |       |  |
| Units: Subjects   |  |       |  |
| In utero  | 0  | 0     |  |
| Preterm newborn infants (gestational age < 37 wks)  | 0  | 0     |  |
| Newborns (0-27 days)  | 0  | 0     |  |
| Infants and toddlers (28 days-23 months)  | 0  | 0     |  |
| Children (2-11 years)   | 0  | 0     |  |
| Adolescents (12-17 years)   | 0  | 0     |  |
| Adults (18-64 years)  | 19   | 103   |  |
| From 65-84 years  | 3  | 68    |  |
| 85 years and over   | 0  | 3     |  |
| Age Continuous  |  |       |  |
| <p>Treated Set (TS): Included all patients who were dispensed study treatment and were documented to have taken at least one dose of the study treatment.</p> <p>For Phase Ib-Schedule B SCLC, Phase Ib-Schedule B mCRPC, DMC lowered the dose of SCLC and mCRPC, thus patients treated prior the decision took 2.5mg BI 894999 and patients treated after the decision received 2mg. For Phase Ib - Schedule C NC, the dose was lowered since DMC reclaimed the MTD as 6/3mg after 1 patient already treated with 7/3.5mg.</p> |  |       |  |
| Units: years  |  |       |  |
| arithmetic mean   | 40.5   |       |  |
| standard deviation  | ± 16.5   | -     |  |

|   |    |     |  |
|---|----|-----|--|
| Sex: Female, Male   |    |     |  |
| <p>Treated Set (TS): Included all patients who were dispensed study treatment and were documented to have taken at least one dose of the study treatment.</p> <p>For Phase Ib-Schedule B SCLC, Phase Ib-Schedule B mCRPC, DMC lowered the dose of SCLC and mCRPC, thus patients treated prior the decision took 2.5mg BI 894999 and patients treated after the decision received 2mg. For Phase Ib - Schedule C NC, the dose was lowered since DMC reclaimed the MTD as 6/3mg after 1 patient already treated with 7/3.5mg.</p> |    |     |  |
| Units: Participants   |    |     |  |
| Female  | 8  | 61  |  |
| Male  | 14 | 113 |  |
| Race (NIH/OMB)  |    |     |  |
| <p>Treated Set (TS): Included all patients who were dispensed study treatment and were documented to have taken at least one dose of the study treatment.</p> <p>For Phase Ib-Schedule B SCLC, Phase Ib-Schedule B mCRPC, DMC lowered the dose of SCLC and mCRPC, thus patients treated prior the decision took 2.5mg BI 894999 and patients treated after the decision received 2mg. For Phase Ib - Schedule C NC, the dose was lowered since DMC reclaimed the MTD as 6/3mg after 1 patient already treated with 7/3.5mg.</p> |    |     |  |
| Units: Subjects   |    |     |  |
| American Indian or Alaska Native  | 0  | 0   |  |
| Asian   | 1  | 4   |  |
| Native Hawaiian or Other Pacific Islander   | 0  | 0   |  |
| Black or African American   | 1  | 3   |  |
| White   | 16 | 140 |  |
| More than one race  | 0  | 0   |  |
| Unknown or Not Reported   | 4  | 27  |  |
| Ethnicity (NIH/OMB)   |    |     |  |
| <p>Treated Set (TS): Included all patients who were dispensed study treatment and were documented to have taken at least one dose of the study treatment.</p> <p>For Phase Ib-Schedule B SCLC, Phase Ib-Schedule B mCRPC, DMC lowered the dose of SCLC and mCRPC, thus patients treated prior the decision took 2.5mg BI 894999 and patients treated after the decision received 2mg. For Phase Ib - Schedule C NC, the dose was lowered since DMC reclaimed the MTD as 6/3mg after 1 patient already treated with 7/3.5mg.</p> |    |     |  |
| Units: Subjects   |    |     |  |
| Hispanic or Latino  | 1  | 6   |  |
| Not Hispanic or Latino  | 17 | 143 |  |
| Unknown or Not Reported   | 4  | 25  |  |

## End points

### End points reporting groups

|  |   |
|--|---|
| Reporting group title  | Phase Ia - Schedule A: 0.2 mg BI 894999 |
| Reporting group description:   |   |
| Adult patients with a confirmed diagnosis of advanced, unresectable and/or metastatic malignant solid tumours who had failed conventional treatment or for whom no therapy of proven efficacy existed or who were not amenable to standard therapies were administered orally 0.2 milligram (mg) of BI 894999 once daily, in the morning, after an overnight fast, 1 hour before breakfast with at least 250 milliliter (mL) of water. Schedule A was a continuous daily intake in cycles of 21 days.  |   |
| Reporting group title  | Phase Ia - Schedule A: 0.5 mg BI 894999 |
| Reporting group description:   |   |
| Adult patients with a confirmed diagnosis of advanced, unresectable and/or metastatic malignant solid tumours who had failed conventional treatment or for whom no therapy of proven efficacy existed or who were not amenable to standard therapies were administered orally 0.5 milligram (mg) of BI 894999 once daily, in the morning, after an overnight fast, 1 hour before breakfast with at least 250 milliliter (mL) of water. Schedule A was a continuous daily intake in cycles of 21 days.  |   |
| Reporting group title  | Phase Ia - Schedule A: 1 mg BI 894999   |
| Reporting group description:   |   |
| Adult patients with a confirmed diagnosis of advanced, unresectable and/or metastatic malignant solid tumours who had failed conventional treatment or for whom no therapy of proven efficacy existed or who were not amenable to standard therapies were administered orally 1 milligram (mg) of BI 894999 once daily, in the morning, after an overnight fast, 1 hour before breakfast with at least 250 milliliter (mL) of water. Schedule A was a continuous daily intake in cycles of 21 days.  |   |
| Reporting group title  | Phase Ia - Schedule A: 1.5 mg BI 894999 |
| Reporting group description:   |   |
| Adult patients with a confirmed diagnosis of advanced, unresectable and/or metastatic malignant solid tumours who had failed conventional treatment or for whom no therapy of proven efficacy existed or who were not amenable to standard therapies were administered orally 1.5 milligram (mg) of BI 894999 once daily, in the morning, after an overnight fast, 1 hour before breakfast with at least 250 milliliter (mL) of water. Schedule A was a continuous daily intake in cycles of 21 days.  |   |
| Reporting group title  | Phase Ia - Schedule A: 2 mg BI 894999   |
| Reporting group description:   |   |
| Adult patients with a confirmed diagnosis of advanced, unresectable and/or metastatic malignant solid tumours who had failed conventional treatment or for whom no therapy of proven efficacy existed or who were not amenable to standard therapies were administered orally 2 milligram (mg) of BI 894999 once daily, in the morning, after an overnight fast, 1 hour before breakfast with at least 250 milliliter (mL) of water. Schedule A was a continuous daily intake in cycles of 21 days.  |   |
| Reporting group title  | Phase Ia - Schedule A: 5 mg BI 894999   |
| Reporting group description:   |   |
| Adult patients with a confirmed diagnosis of advanced, unresectable and/or metastatic malignant solid tumours who had failed conventional treatment or for whom no therapy of proven efficacy existed or who were not amenable to standard therapies were administered orally 5 milligram (mg) of BI 894999 once daily, in the morning, after an overnight fast, 1 hour before breakfast with at least 250 milliliter (mL) of water. Schedule A was a continuous daily intake in cycles of 21 days.  |   |
| Reporting group title  | Phase Ia - Schedule B: 1.5 mg BI 894999 |
| Reporting group description:   |   |
| Adult patients with a confirmed diagnosis of advanced, unresectable and/or metastatic malignant solid tumours who had failed conventional treatment or for whom no therapy of proven efficacy existed or who were not amenable to standard therapies were administered orally 1.5 milligram (mg) of BI 894999 once daily, in the morning, after an overnight fast, 1 hour before breakfast with at least 250 milliliter (mL) of water. Schedule B was a continuous intake for 14 days followed by one week off treatment in cycles of 21 days. |   |
| Reporting group title  | Phase Ia - Schedule B: 2 mg BI 894999   |
| Reporting group description:   |   |
| Adult patients with a confirmed diagnosis of advanced, unresectable and/or metastatic malignant solid tumours who had failed conventional treatment or for whom no therapy of proven efficacy existed or who were not amenable to standard therapies were administered orally 2 milligram (mg) of BI 894999 once daily, in the morning, after an overnight fast, 1 hour before breakfast with at least 250 milliliter (mL) of water. Schedule B was a continuous intake for 14 days followed by one week off treatment in                      |   |

cycles of 21 days.

|                       |   |
|-----------------------|---|
| Reporting group title | Phase Ia - Schedule B: 2.5 mg BI 894999 |
|-----------------------|---|

Reporting group description:

Adult patients with a confirmed diagnosis of advanced, unresectable and/or metastatic malignant solid tumours who had failed conventional treatment or for whom no therapy of proven efficacy existed or who were not amenable to standard therapies were administered orally 2.5 mg of BI 894999 once daily, in the morning, after an overnight fast, 1 hour before breakfast with at least 250 milliliter (mL) of water. Schedule B was a continuous intake for 14 days followed by one week off treatment in cycles of 21 days.

|                       |   |
|-----------------------|---|
| Reporting group title | Phase Ia - Schedule C: 5/2.5 mg BI 894999 |
|-----------------------|---|

Reporting group description:

Adult patients with a confirmed diagnosis of advanced, unresectable and/or metastatic malignant solid tumours who had failed conventional treatment or for whom no therapy of proven efficacy existed or who were not amenable to standard therapies were administered orally once daily on Day 1 and on Day 15 of each cycle a loading dose of 5 milligram (mg) of BI 894999, followed by six days daily intake of the maintenance dose of 2.5 mg of BI 894999 once daily, followed by one week off, repeated every two weeks in cycles of 28 days (Schedule C). The loading and the maintenance dose were administered in the morning, after an overnight fast, 1 hour before breakfast with at least 250 milliliter (mL) of water.

|                       |   |
|-----------------------|---|
| Reporting group title | Phase Ia - Schedule C: 6/3 mg BI 894999 |
|-----------------------|---|

Reporting group description:

Adult patients with a confirmed diagnosis of advanced, unresectable and/or metastatic malignant solid tumours who had failed conventional treatment or for whom no therapy of proven efficacy existed or who were not amenable to standard therapies were administered orally once daily on Day 1 and on Day 15 of each cycle a loading dose of 6 milligram (mg) of BI 894999, followed by six days daily intake of the maintenance dose of 3 mg of BI 894999 once daily, followed by one week off, repeated every two weeks in cycles of 28 days (Schedule C). The loading and the maintenance dose were administered in the morning, after an overnight fast, 1 hour before breakfast with at least 250 milliliter (mL) of water.

|                       |   |
|-----------------------|---|
| Reporting group title | Phase Ia - Schedule C: 7/3.5 mg BI 894999 |
|-----------------------|---|

Reporting group description:

Adult patients with a confirmed diagnosis of advanced, unresectable and/or metastatic malignant solid tumours who had failed conventional treatment or for whom no therapy of proven efficacy existed or who were not amenable to standard therapies were administered orally once daily on Day 1 and on Day 15 of each cycle a loading dose of 7 milligram (mg) of BI 894999, followed by six days daily intake of the maintenance dose of 3.5 mg of BI 894999 once daily, followed by one week off, repeated every two weeks in cycles of 28 days (Schedule C). The loading and the maintenance dose were administered in the morning, after an overnight fast, 1 hour before breakfast with at least 250 milliliter (mL) of water.

|                       |  |
|-----------------------|--|
| Reporting group title | Phase Ia - Schedule B: 1.5 mg BI 894999 (DLBCL patients) |
|-----------------------|--|

Reporting group description:

Adult patients with histologically confirmed diagnosis of diffuse large B-cell lymphoma (DLBCL) were administered orally 1.5 milligram (mg) of BI 894999 once daily, in the morning, after an overnight fast, 1 hour before breakfast with at least 250 milliliter (mL) of water. Schedule B was a continuous intake for 14 days followed by one week off treatment in cycles of 21 days.

|                       |  |
|-----------------------|--|
| Reporting group title | Phase Ia - Schedule B: 2 mg BI 894999 (DLBCL patients) |
|-----------------------|--|

Reporting group description:

Adult patients with histologically confirmed diagnosis of diffuse large B-cell lymphoma (DLBCL) were administered orally 2 milligram (mg) of BI 894999 once daily, in the morning, after an overnight fast, 1 hour before breakfast with at least 250 milliliter (mL) of water. Schedule B was a continuous intake for 14 days followed by one week off treatment in cycles of 21 days.

|                       |  |
|-----------------------|--|
| Reporting group title | Phase Ia - Schedule B: 2.5 mg BI 894999 (DLBCL patients) |
|-----------------------|--|

Reporting group description:

Adult patients with histologically confirmed diagnosis of diffuse large B-cell lymphoma (DLBCL) were administered orally 2.5 milligram (mg) of BI 894999 once daily, in the morning, after an overnight fast, 1 hour before breakfast with at least 250 milliliter (mL) of water. Schedule B was a continuous intake for 14 days followed by one week off treatment in cycles of 21 days.

|                       |  |
|-----------------------|--|
| Reporting group title | Phase Ia - Schedule C: 4/2 mg BI 894999 (DLBCL patients) |
|-----------------------|--|

Reporting group description:

Adult patients with histologically confirmed diagnosis of diffuse large B-cell lymphoma (DLBCL) were administered orally once daily on Day 1 and on Day 15 of each cycle a loading dose of 4 milligram (mg) of BI 894999, followed by six days daily intake of the maintenance dose of 2 mg of BI 894999 once daily, followed by one week off, repeated every two weeks in cycles of 28 days (Schedule C). The loading and the maintenance dose were administered in the morning, after an overnight fast, 1 hour before breakfast with at least 250 milliliter (mL) of water.

|                       |  |
|-----------------------|--|
| Reporting group title | Phase Ia - Schedule C: BI 894999 5/2.5 mg (DLBCL patients) |
|-----------------------|--|

Reporting group description:

Adult patients with histologically confirmed diagnosis of diffuse large B-cell lymphoma (DLBCL) were administered orally once daily on Day 1 and on Day 15 of each cycle a loading dose of 5 milligram (mg) of BI 894999, followed by six days daily intake of the maintenance dose of 2.5 mg of BI 894999, followed by one week off, repeated every two weeks in cycles of 28 days (Schedule C). The loading and the maintenance dose were administered in the morning, after an overnight fast, 1 hour before breakfast with at least 250 milliliter (mL) of water.

|                       |  |
|-----------------------|--|
| Reporting group title | Phase Ib - Schedule B: 2 or 2.5 mg BI 894999 (SCLC patients) |
|-----------------------|--|

Reporting group description:

This arm included adult patients diagnosed with small cell lung cancer (SCLC).

SCLC patients were initially administered 2.5 mg of BI 894999. BI 894999 administration was performed in the morning, after an overnight fast, 1 hour before breakfast with at least 250 milliliter (mL) of water according to Schedule B (continuous intake for 14 days followed by one week off treatment in cycles of 21 days).

The Data Monitoring Committee decided on 28 November 2018 to lower the 2.5 mg BI 894999 dose due to safety concerns to 2mg, therefore patients treated before the decision were administered 2.5mg, and patients treated after the decision were administered 2mg.

|                       |  |
|-----------------------|--|
| Reporting group title | Phase Ib - Schedule B: 2.5 mg BI 894999 (CRC patients) |
|-----------------------|--|

Reporting group description:

Adult patients diagnosed with colorectal cancer (CRC) were administered orally 2.5 milligram (mg) of BI 894999. BI 894999 administration was performed in the morning, after an overnight fast, 1 hour before breakfast with at least 250 milliliter (mL) of water according to Schedule B (continuous intake for 14 days followed by one week off treatment in cycles of 21 days).

|                       |   |
|-----------------------|---|
| Reporting group title | Phase Ib - Schedule B: 2 or 2.5 mg BI 894999 (mCRPC patients) |
|-----------------------|---|

Reporting group description:

This arm included adult patients diagnosed with metastatic castrate resistant prostate cancer (mCRPC). MCRPC patients were initially administered 2.5 mg of BI 894999. BI 894999 administration was performed in the morning, after an overnight fast, 1 hour before breakfast with at least 250 milliliter (mL) of water according to Schedule B (continuous intake for 14 days followed by one week off treatment in cycles of 21 days).

The Data Monitoring Committee decided on 28 November 2018 to lower the 2.5 mg BI 894999 dose due to safety concerns to 2mg, therefore patients treated before the decision were administered 2.5mg, and patients treated after the decision were administered 2mg.

|                       |   |
|-----------------------|---|
| Reporting group title | Phase Ib - Schedule B: 2.5 mg BI 894999 (NC patients) |
|-----------------------|---|

Reporting group description:

Adult patients diagnosed with NUT carcinoma (NC) were administered orally 2.5 milligram (mg) of BI 894999 once daily, in the morning, after an overnight fast, 1 hour before breakfast with at least 250 milliliter (mL) of water. Schedule B was a continuous intake for 14 days followed by one week off treatment in cycles of 21 days. The 2.5 mg dose could be reduced to 2 mg in case of adverse events.

|                       |  |
|-----------------------|--|
| Reporting group title | Phase Ib - Schedule C: 6/3 or 7/3.5 mg BI 894999 (NC patients) |
|-----------------------|--|

Reporting group description:

This arm included adult patients diagnosed with NUT carcinoma (NC).

The DMC reclaimed the maximum tolerated dose (MTD) as 6/3mg on 08 July 2020 after 1 patient was already treated with 7/3.5mg, so the first patient in NC and all the following patients were treated with 6/3mg.

Patients in were administered orally once daily on Day 1 and on Day 15 of each cycle a loading dose of 6 milligram (mg) of BI 894999, followed by six days intake of the maintenance dose of 3 mg of BI 894999 once daily, followed by one week off, repeated every two weeks in cycles of 28 days (Schedule C).

|                            |   |
|----------------------------|---|
| Subject analysis set title | Phase Ib - Schedule C: BI 894999 7/3.5 mg (NC patients) |
|----------------------------|---|

|                           |              |
|---------------------------|--------------|
| Subject analysis set type | Per protocol |
|---------------------------|--------------|

Subject analysis set description:

Adult patients diagnosed with NUT carcinoma (NC) were administered orally once daily on Day 1 and on Day 15 of each cycle a loading dose of 7 milligram (mg) of BI 894999, followed by six days intake of the maintenance dose of 3.5 mg of BI 894999 once daily, followed by one week off, repeated every two weeks in cycles of 28 days (Schedule C). The loading and the maintenance dose were administered in the morning, after an overnight fast, 1 hour before breakfast with at least 250 milliliter (mL) of water. This Subject Analysis Set is reporting descriptive statistics for the endpoints AUC0-24 and Cmax.

|                            |  |
|----------------------------|--|
| Subject analysis set title | Phase Ib - Schedule B: BI 894999 2 mg (solid tumours+NC) |
|----------------------------|--|

|                           |              |
|---------------------------|--------------|
| Subject analysis set type | Per protocol |
|---------------------------|--------------|

Subject analysis set description:

Adult patients diagnosed with one of the following cancer types small cell lung cancer (SCLC); metastatic castrate resistant prostate cancer (mCRPC); NUT carcinoma (NC) were administered orally 2 milligram (mg) of BI 894999 once daily, in the morning, after an overnight fast, 1 hour before breakfast with at least 250 milliliter (mL) of water. Schedule B was a continuous intake for 14 days followed by one week off treatment in cycles of 21 days.

This Subject Analysis Set is reporting descriptive statistics for the endpoints AUC0-24 and Cmax.

|                            |  |
|----------------------------|--|
| Subject analysis set title | Phase Ib - Schedule B: BI 894999 2.5 mg (solid tumours + NC) |
| Subject analysis set type  | Per protocol   |

Subject analysis set description:

Adult patients diagnosed with one of the following cancer types small cell lung cancer (SCLC); metastatic castrate resistant prostate cancer (mCRPC); colorectal cancer (CRC); NUT carcinoma (NC) were administered orally 2.5 milligram (mg) of BI 894999, in the morning, after an overnight fast, 1 hour before breakfast with at least 250 milliliter (mL) of water. Schedule B was a continuous intake for 14 days followed by one week off treatment in cycles of 21 days.

This Subject Analysis Set is reporting descriptive statistics for the endpoint AUC0-24.

|                            |   |
|----------------------------|---|
| Subject analysis set title | Phase Ib - Schedule C: BI 894999 6/3 mg (NC patients) |
| Subject analysis set type  | Per protocol  |

Subject analysis set description:

Adult patients diagnosed with NUT carcinoma (NC) were administered orally once daily on Day 1 and on Day 15 of each cycle a loading dose of 6 milligram (mg) of BI 894999, followed by six days intake of the maintenance dose of 3 mg of BI 894999 once daily, followed by one week off, repeated every two weeks in cycles of 28 days (Schedule C).

This Subject Analysis Set is reporting descriptive statistics for the endpoint AUC0-24.

|                            |  |
|----------------------------|--|
| Subject analysis set title | Phase Ib - Schedule B: BI 894999 2.5 mg (solid tumours + NC) |
| Subject analysis set type  | Per protocol   |

Subject analysis set description:

Adult patients diagnosed with one of the following cancer types small cell lung cancer (SCLC); metastatic castrate resistant prostate cancer (mCRPC); colorectal cancer (CRC); NUT carcinoma (NC) were administered orally 2.5 milligram (mg) of BI 894999, in the morning, after an overnight fast, 1 hour before breakfast with at least 250 milliliter (mL) of water. Schedule B was a continuous intake for 14 days followed by one week off treatment in cycles of 21 days.

This Subject Analysis Set is reporting descriptive statistics for the endpoint Cmax.

|                            |   |
|----------------------------|---|
| Subject analysis set title | Phase Ib - Schedule C: BI 894999 6/3 mg (NC patients) |
| Subject analysis set type  | Per protocol  |

Subject analysis set description:

Adult patients diagnosed with NUT carcinoma (NC) were administered orally once daily on Day 1 and on Day 15 of each cycle a loading dose of 6 milligram (mg) of BI 894999, followed by six days intake of the maintenance dose of 3 mg of BI 894999 once daily, followed by one week off, repeated every two weeks in cycles of 28 days (Schedule C).

This Subject Analysis Set is reporting descriptive statistics for the endpoint Cmax.

|                            |   |
|----------------------------|---|
| Subject analysis set title | Phase Ib - Schedule C: BI 894999 7/3.5 mg (NC patients) |
| Subject analysis set type  | Per protocol  |

Subject analysis set description:

Adult patients diagnosed with NUT carcinoma (NC) were administered orally once daily on Day 1 and on Day 15 of each cycle a loading dose of 7 milligram (mg) of BI 894999, followed by six days intake of the maintenance dose of 3.5 mg of BI 894999 once daily, followed by one week off, repeated every two weeks in cycles of 28 days (Schedule C). The loading and the maintenance dose were administered in the morning, after an overnight fast, 1 hour before breakfast with at least 250 milliliter (mL) of water.

This subject analysis set is reporting descriptive statistics for the endpoints AUC<sub>tr, ss</sub> and Cmax, ss.

|                            |  |
|----------------------------|--|
| Subject analysis set title | Phase Ib - Schedule B: 2 mg BI 894999 (NC patients only) |
| Subject analysis set type  | Per protocol   |

Subject analysis set description:

Adult patients diagnosed with NUT carcinoma (NC) were administered during the first cycle 2.5 milligram (mg) BI 894999 according to Schedule B and then the dosage was decreased at steady state to 2 mg of BI 894999 once daily, in the morning, after an overnight fast, 1 hour before breakfast with at least 250 milliliter (mL) of water. Schedule B was a continuous intake for 14 days followed by one week off treatment in cycles of 21 days.

This subject analysis set is reporting descriptive statistics for the endpoints AUC<sub>tr, ss</sub> and Cmax, ss.

|                            |  |
|----------------------------|--|
| Subject analysis set title | Phase Ib - Schedule B: BI 894999 2 mg (solid tumours + NC) |
| Subject analysis set type  | Per protocol   |

Subject analysis set description:

Adult patients diagnosed with one of the following cancer types small cell lung cancer (SCLC); metastatic castrate resistant prostate cancer (mCRPC); NUT carcinoma (NC) were administered orally 2 milligram (mg) of BI 894999 once daily, in the morning, after an overnight fast, 1 hour before breakfast with at least 250 milliliter (mL) of water. Schedule B was a continuous intake for 14 days followed by one week off treatment in cycles of 21 days.

This subject analysis set is reporting descriptive statistics for the endpoints AUC<sub>T</sub>, ss and C<sub>max</sub>, ss.

|                            |  |
|----------------------------|--|
| Subject analysis set title | Phase Ib - Schedule B: BI 894999 2.5 mg (solid tumours + NC) |
| Subject analysis set type  | Per protocol   |

Subject analysis set description:

Adult patients diagnosed with one of the following cancer types small cell lung cancer (SCLC); metastatic castrate resistant prostate cancer (mCRPC); colorectal cancer (CRC); NUT carcinoma (NC) were administered orally 2.5 milligram (mg) of BI 894999, in the morning, after an overnight fast, 1 hour before breakfast with at least 250 milliliter (mL) of water. Schedule B was a continuous intake for 14 days followed by one week off treatment in cycles of 21 days.

This subject analysis set is reporting descriptive statistics for the endpoints AUC<sub>T</sub>, ss and C<sub>max</sub>, ss.

|                            |   |
|----------------------------|---|
| Subject analysis set title | Phase Ib - Schedule C: BI 894999 6/3 mg (NC patients) |
| Subject analysis set type  | Per protocol  |

Subject analysis set description:

Adult patients diagnosed with NUT carcinoma (NC) were administered orally once daily on Day 1 and on Day 15 of each cycle a loading dose of 6 milligram (mg) of BI 894999, followed by six days intake of the maintenance dose of 3 mg of BI 894999 once daily, followed by one week off, repeated every two weeks in cycles of 28 days (Schedule C).

This subject analysis set is reporting descriptive statistics for the endpoints AUC<sub>T</sub>, ss and C<sub>max</sub>, ss.

**Primary: Phase Ia: Number of patients with Dose Limiting Toxicities (DLTs) observed in the first cycle**

|                 |   |
|-----------------|---|
| End point title | Phase Ia: Number of patients with Dose Limiting Toxicities (DLTs) observed in the first cycle <sup>[1][2]</sup> |
|-----------------|---|

End point description:

The following drug related adverse events (AEs) qualified as DLT:

- any Common Terminology Criteria for AEs (CTCAE) grade  $\geq 3$  non haematological toxicity considered related to trial medication with the following exceptions:

-- inadequately treated nausea, vomiting or diarrhoea. For fatigue, if present at baseline, there had to be an increase of  $\geq 2$  grades

-- electrolytes abnormalities that were corrected within 72 hours with treatment

- any haematologic AE related to the trial medication defined as follows:

-- CTCAE grade  $\geq 4$  neutropenia lasting  $\geq 7$  days and/or complicated by infection, or

-- CTCAE grade  $\geq 4$  thrombocytopenia, or

-- CTCAE grade  $\geq 3$  thrombocytopenia coupled with grade  $\geq 2$  of bleeding, or

-- febrile neutropenia CTCAE grade 3 or higher.

- any other drug-related AE preventing the patient from taking his treatment according to given schedule.

Maximum Tolerated Dose (MTD) Evaluation Set: Included all patients in the TS of Phase 1a who were not replaced for the MTD determination.

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

End point timeframe:

First treatment cycle (the first 21 days for Schedules A and B, the first 28 days for Schedule C).

Notes:

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

Justification: Endpoint was analyzed only descriptively.

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

Justification: Endpoint was specified only for the participants of the Phase1a.



| End point values            | Phase Ia -<br>Schedule A:<br>0.2 mg BI<br>894999 | Phase Ia -<br>Schedule A:<br>0.5 mg BI<br>894999 | Phase Ia -<br>Schedule A: 1<br>mg BI 894999 | Phase Ia -<br>Schedule A:<br>1.5 mg BI<br>894999 |
|-----------------------------|--|--|---|--|
| Subject group type          | Reporting group                                  | Reporting group                                  | Reporting group                             | Reporting group                                  |
| Number of subjects analysed | 2 <sup>[3]</sup>                                 | 2 <sup>[4]</sup>                                 | 3 <sup>[5]</sup>                            | 6 <sup>[6]</sup>                                 |
| Units: Participants         | 0  | 0  | 0   | 0  |

Notes:

[3] - Maximum Tolerated Dose (MTD) Evaluation Set (MTDS)

[4] - MTDS

[5] - MTDS

[6] - MTDS

| End point values            | Phase Ia -<br>Schedule A: 2<br>mg BI 894999 | Phase Ia -<br>Schedule A: 5<br>mg BI 894999 | Phase Ia -<br>Schedule B:<br>1.5 mg BI<br>894999 | Phase Ia -<br>Schedule B: 2<br>mg BI 894999 |
|-----------------------------|---|---|--|---|
| Subject group type          | Reporting group                             | Reporting group                             | Reporting group                                  | Reporting group                             |
| Number of subjects analysed | 6 <sup>[7]</sup>                            | 2 <sup>[8]</sup>                            | 5 <sup>[9]</sup>                                 | 6 <sup>[10]</sup>                           |
| Units: Participants         | 3   | 2   | 1  | 0   |

Notes:

[7] - MTDS

[8] - MTDS

[9] - MTDS

[10] - MTDS

| End point values            | Phase Ia -<br>Schedule B:<br>2.5 mg BI<br>894999 | Phase Ia -<br>Schedule C:<br>5/2.5 mg BI<br>894999 | Phase Ia -<br>Schedule C:<br>6/3 mg BI<br>894999 | Phase Ia -<br>Schedule C:<br>7/3.5 mg BI<br>894999 |
|-----------------------------|--|--|--|--|
| Subject group type          | Reporting group                                  | Reporting group                                    | Reporting group                                  | Reporting group                                    |
| Number of subjects analysed | 12 <sup>[11]</sup>                               | 3 <sup>[12]</sup>                                  | 12 <sup>[13]</sup>                               | 10 <sup>[14]</sup>                                 |
| Units: Participants         | 2  | 0  | 2  | 4  |

Notes:

[11] - MTDS

[12] - MTDS

[13] - MTDS

[14] - MTDS

| End point values            | Phase Ia -<br>Schedule B:<br>1.5 mg BI<br>894999 (DLBCL<br>patients) | Phase Ia -<br>Schedule B: 2<br>mg BI 894999<br>(DLBCL<br>patients) | Phase Ia -<br>Schedule B:<br>2.5 mg BI<br>894999 (DLBCL<br>patients) | Phase Ia -<br>Schedule C:<br>4/2 mg BI<br>894999 (DLBCL<br>patients) |
|-----------------------------|--|--|--|--|
| Subject group type          | Reporting group  | Reporting group  | Reporting group  | Reporting group  |
| Number of subjects analysed | 8 <sup>[15]</sup>  | 3 <sup>[16]</sup>  | 2 <sup>[17]</sup>  | 2 <sup>[18]</sup>  |
| Units: Participants         | 1  | 1  | 2  | 0  |

Notes:

[15] - MTDS

[16] - MTDS

[17] - MTDS

[18] - MTDS

| End point values | Phase Ia -<br>Schedule C: BI<br>894999 5/2.5<br>mg (DLBCL |  |  |  |
|------------------|---|--|--|--|
|------------------|---|--|--|--|

|                             |                   |  |  |  |
|-----------------------------|-------------------|--|--|--|
|                             | patients)         |  |  |  |
| Subject group type          | Reporting group   |  |  |  |
| Number of subjects analysed | 2 <sup>[19]</sup> |  |  |  |
| Units: Participants         | 0                 |  |  |  |

Notes:

[19] - MTDS

## Statistical analyses

No statistical analyses for this end point

### Primary: Phase Ib: Number of patients with Dose Limiting Toxicities (DLTs) observed during the on-treatment period

|                 |   |
|-----------------|---|
| End point title | Phase Ib: Number of patients with Dose Limiting Toxicities (DLTs) observed during the on-treatment period <sup>[20][21]</sup> |
|-----------------|---|

End point description:

The following drug related adverse events (AEs) qualified as DLT:

- any Common Terminology Criteria for Adverse Events (CTCAE) grade  $\geq 3$  non haematological toxicity considered related to trial medication with the following exceptions:
- inadequately treated nausea, vomiting or diarrhoea. For fatigue, if present at baseline, there had to be an increase of  $\geq 2$  grades
- electrolytes abnormalities that were corrected within 72 hours with treatment
- any haematologic AE related to the trial medication defined as follows:
- CTCAE grade  $\geq 4$  neutropenia lasting  $\geq 7$  days and/or complicated by infection, or
- CTCAE grade  $\geq 4$  thrombocytopenia, or
- CTCAE grade  $\geq 3$  thrombocytopenia coupled with grade  $\geq 2$  of bleeding, or
- febrile neutropenia CTCAE grade 3 or higher.
- any other drug-related AE preventing the patient from taking his treatment according to the given schedule.

Treated Set in Phase Ib dose expansion (TS PhIb): All patients in the TS who were treated in Phase Ib.

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

End point timeframe:

Date of the first administration of study treatment until date of the last administration of study treatment + 30 days residual effect period, up to 883 days.

Notes:

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

Justification: Endpoint was analyzed only descriptively.

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

Justification: Endpoint was specified only for the participants of the Phase 1b.

| End point values            | Phase Ib - Schedule B: 2 or 2.5 mg BI 894999 (SCLC patients) | Phase Ib - Schedule B: 2.5 mg BI 894999 (CRC patients) | Phase Ib - Schedule B: 2 or 2.5 mg BI 894999 (mCRPC patients) | Phase Ib - Schedule B: 2.5 mg BI 894999 (NC patients) |
|-----------------------------|--|--|---|---|
| Subject group type          | Reporting group  | Reporting group  | Reporting group   | Reporting group                                       |
| Number of subjects analysed | 12 <sup>[22]</sup>   | 14 <sup>[23]</sup>                                     | 11 <sup>[24]</sup>  | 20 <sup>[25]</sup>                                    |
| Units: Participants         | 3  | 2  | 7   | 2   |

Notes:

[22] - Treated Set (TS) in Phase Ib dose expansion (TS PhIb).

[23] - TS PhIb

[24] - TS PhIb

[25] - TS PhIb

|                             |  |  |  |  |
|-----------------------------|--|--|--|--|
| <b>End point values</b>     | Phase Ib -<br>Schedule C:<br>6/3 or 7/3.5<br>mg BI 894999<br>(NC patients) |  |  |  |
| Subject group type          | Reporting group  |  |  |  |
| Number of subjects analysed | 22 <sup>[26]</sup>   |  |  |  |
| Units: Participants         | 3  |  |  |  |

Notes:

[26] - TS PhIb

## Statistical analyses

No statistical analyses for this end point

## Secondary: Phase Ia: Number of patients with Dose Limiting Toxicities (DLTs) observed during the on-treatment period

|                 |   |
|-----------------|---|
| End point title | Phase Ia: Number of patients with Dose Limiting Toxicities (DLTs) observed during the on-treatment period <sup>[27]</sup> |
|-----------------|---|

End point description:

The following drug related adverse events (AEs) qualified as DLT:

- any Common Terminology Criteria for AEs (CTCAE) grade  $\geq 3$  non haematological toxicity considered related to trial medication with the following exceptions:
  - inadequately treated nausea, vomiting or diarrhoea. For fatigue, if present at baseline, there had to be an increase of  $\geq 2$  grades
  - electrolytes abnormalities that were corrected within 72 hours with treatment
- any haematologic AE related to the trial medication defined as follows:
  - CTCAE grade  $\geq 4$  neutropenia lasting  $\geq 7$  days and/or complicated by infection, or
  - CTCAE grade  $\geq 4$  thrombocytopenia, or
  - CTCAE grade  $\geq 3$  thrombocytopenia coupled with grade  $\geq 2$  of bleeding, or
  - febrile neutropenia CTCAE grade 3 or higher.
- any other drug-related AE preventing the patient from taking his treatment according to the given schedule.

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

End point timeframe:

Date of the first administration of study treatment until date of the last administration of study treatment + 30 days residual effect period, up to 463 days.

Notes:

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

Justification: Endpoint was specified only for the participants of the Phase 1a.

|                             |  |  |   |  |
|-----------------------------|--|--|---|--|
| <b>End point values</b>     | Phase Ia -<br>Schedule A:<br>0.2 mg BI<br>894999 | Phase Ia -<br>Schedule A:<br>0.5 mg BI<br>894999 | Phase Ia -<br>Schedule A: 1<br>mg BI 894999 | Phase Ia -<br>Schedule A:<br>1.5 mg BI<br>894999 |
| Subject group type          | Reporting group                                  | Reporting group                                  | Reporting group                             | Reporting group                                  |
| Number of subjects analysed | 2 <sup>[28]</sup>                                | 2 <sup>[29]</sup>                                | 3 <sup>[30]</sup>                           | 6 <sup>[31]</sup>                                |
| Units: Participants         | 0  | 0  | 0   | 2  |

Notes:

[28] - Treated Set in Phase 1a

[29] - Treated Set in Phase 1a

[30] - Treated Set in Phase 1a

[31] - Treated Set in Phase 1a

|                         |   |   |  |   |
|-------------------------|---|---|--|---|
| <b>End point values</b> | Phase Ia -<br>Schedule A: 2<br>mg BI 894999 | Phase Ia -<br>Schedule A: 5<br>mg BI 894999 | Phase Ia -<br>Schedule B:<br>1.5 mg BI | Phase Ia -<br>Schedule B: 2<br>mg BI 894999 |
|-------------------------|---|---|--|---|

|                             |                   |                   |                   |                   |
|-----------------------------|-------------------|-------------------|-------------------|-------------------|
|                             |                   |                   | 894999            |                   |
| Subject group type          | Reporting group   | Reporting group   | Reporting group   | Reporting group   |
| Number of subjects analysed | 6 <sup>[32]</sup> | 2 <sup>[33]</sup> | 6 <sup>[34]</sup> | 6 <sup>[35]</sup> |
| Units: Participants         | 4                 | 2                 | 1                 | 0                 |

Notes:

[32] - Treated Set in Phase 1a

[33] - Treated Set in Phase 1a

[34] - Treated Set in Phase 1a

[35] - Treated Set in Phase 1a

|                             |  |  |  |  |
|-----------------------------|--|--|--|--|
| <b>End point values</b>     | Phase Ia -<br>Schedule B:<br>2.5 mg BI<br>894999 | Phase Ia -<br>Schedule C:<br>5/2.5 mg BI<br>894999 | Phase Ia -<br>Schedule C:<br>6/3 mg BI<br>894999 | Phase Ia -<br>Schedule C:<br>7/3.5 mg BI<br>894999 |
| Subject group type          | Reporting group                                  | Reporting group                                    | Reporting group                                  | Reporting group                                    |
| Number of subjects analysed | 13 <sup>[36]</sup>                               | 4 <sup>[37]</sup>                                  | 15 <sup>[38]</sup>                               | 12 <sup>[39]</sup>                                 |
| Units: Participants         | 3  | 1  | 3  | 4  |

Notes:

[36] - Treated Set in Phase 1a

[37] - Treated Set in Phase 1a

[38] - Treated Set in Phase 1a

[39] - Treated Set in Phase 1a

|                             |  |  |  |  |
|-----------------------------|--|--|--|--|
| <b>End point values</b>     | Phase Ia -<br>Schedule B:<br>1.5 mg BI<br>894999 (DLBCL<br>patients) | Phase Ia -<br>Schedule B: 2<br>mg BI 894999<br>(DLBCL<br>patients) | Phase Ia -<br>Schedule B:<br>2.5 mg BI<br>894999 (DLBCL<br>patients) | Phase Ia -<br>Schedule C:<br>4/2 mg BI<br>894999 (DLBCL<br>patients) |
| Subject group type          | Reporting group  | Reporting group  | Reporting group  | Reporting group  |
| Number of subjects analysed | 8 <sup>[40]</sup>  | 4 <sup>[41]</sup>  | 2 <sup>[42]</sup>  | 2 <sup>[43]</sup>  |
| Units: Participants         | 1  | 2  | 2  | 1  |

Notes:

[40] - Treated Set in Phase 1a

[41] - Treated Set in Phase 1a

[42] - Treated Set in Phase 1a

[43] - Treated Set in Phase 1a

|                             |  |  |  |  |
|-----------------------------|--|--|--|--|
| <b>End point values</b>     | Phase Ia -<br>Schedule C: BI<br>894999 5/2.5<br>mg (DLBCL<br>patients) |  |  |  |
| Subject group type          | Reporting group  |  |  |  |
| Number of subjects analysed | 2 <sup>[44]</sup>  |  |  |  |
| Units: Participants         | 2  |  |  |  |

Notes:

[44] - Treated Set in Phase 1a

## Statistical analyses

No statistical analyses for this end point

**Secondary: Phase Ia and Phase Ib: Area under the concentration-time curve of BI 894999 in plasma over the time interval from 0 to 24 hours after administration of the first dose (AUC0-24)**

|                 |  |
|-----------------|--|
| End point title | Phase Ia and Phase Ib: Area under the concentration-time curve of BI 894999 in plasma over the time interval from 0 to 24 hours after administration of the first dose (AUC0-24) <sup>[45]</sup> |
|-----------------|--|

End point description:

Area under the concentration-time curve of BI 894999 in plasma over the time interval from 0 to 24 hours after administration of the first dose (AUC0-24) for Phase Ia and Phase Ib is reported.  
999999=NA- Could not be calculated due to low number of participants with valid AUC0-24 values.

Pharmacokinetic (PK) analysis Set (PKS): Included all patients in the treated set (TS) who have at least one evaluable PK parameters. Only participants with evaluable results for this PK parameter are reported.

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

End point timeframe:

5 minutes (min) before and at 30 min, 1 hour (h), 2h, 3h, 4h, 6h, 8h and 23h55min after administration of first BI 894999 dose on Day 1 of Cycle 1.

Notes:

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

Justification: In phase Ib, solid tumor patients (SCLC, mCRPC, CRC and NC) are combined by dose level (2 or 2.5mg) as data of all solid tumor patients were needed since no differences were expected, but the NC patients alone were differentiated in an additional subgroup as it was the initial indication for BI 894999.

| End point values                                    | Phase Ia - Schedule A: 0.2 mg BI 894999 | Phase Ia - Schedule A: 0.5 mg BI 894999 | Phase Ia - Schedule A: 1 mg BI 894999 | Phase Ia - Schedule A: 1.5 mg BI 894999 |
|---|---|---|---------------------------------------|---|
| Subject group type                                  | Reporting group                         | Reporting group                         | Reporting group                       | Reporting group                         |
| Number of subjects analysed                         | 2                                       | 2                                       | 3                                     | 5                                       |
| Units: nanomole * hour /Liter (nmol*h/L)            |   |   |                                       |   |
| geometric mean (geometric coefficient of variation) | 4.36 (± 21.1)                           | 6.43 (± 2.78)                           | 20.5 (± 16.8)                         | 34.0 (± 69.4)                           |

| End point values                                    | Phase Ia - Schedule A: 2 mg BI 894999 | Phase Ia - Schedule A: 5 mg BI 894999 | Phase Ia - Schedule B: 1.5 mg BI 894999 | Phase Ia - Schedule B: 2 mg BI 894999 |
|---|---------------------------------------|---------------------------------------|---|---------------------------------------|
| Subject group type                                  | Reporting group                       | Reporting group                       | Reporting group                         | Reporting group                       |
| Number of subjects analysed                         | 4                                     | 0 <sup>[46]</sup>                     | 3                                       | 4                                     |
| Units: nanomole * hour /Liter (nmol*h/L)            |                                       |                                       |   |                                       |
| geometric mean (geometric coefficient of variation) | 64.9 (± 71.0)                         | ()                                    | 27.7 (± 81.5)                           | 44.8 (± 34.8)                         |

Notes:

[46] - No subjects in this arm were analyzed for this endpoint.

| End point values                                    | Phase Ia - Schedule B: 2.5 mg BI 894999 | Phase Ia - Schedule C: 5/2.5 mg BI 894999 | Phase Ia - Schedule C: 6/3 mg BI 894999 | Phase Ia - Schedule C: 7/3.5 mg BI 894999 |
|---|---|---|---|---|
| Subject group type                                  | Reporting group                         | Reporting group                           | Reporting group                         | Reporting group                           |
| Number of subjects analysed                         | 11                                      | 4   | 15                                      | 12  |
| Units: nanomole * hour /Liter (nmol*h/L)            |   |   |   |   |
| geometric mean (geometric coefficient of variation) | 51.5 (± 41.7)                           | 123 (± 37.6)                              | 212 (± 45.5)                            | 230 (± 27.3)                              |

of variation)

| End point values                                       | Phase Ia -<br>Schedule B:<br>1.5 mg BI<br>894999 (DLBCL<br>patients) | Phase Ia -<br>Schedule B: 2<br>mg BI 894999<br>(DLBCL<br>patients) | Phase Ia -<br>Schedule B:<br>2.5 mg BI<br>894999 (DLBCL<br>patients) | Phase Ia -<br>Schedule C:<br>4/2 mg BI<br>894999 (DLBCL<br>patients) |
|--|--|--|--|--|
| Subject group type                                     | Reporting group  | Reporting group  | Reporting group  | Reporting group  |
| Number of subjects analysed                            | 7  | 4  | 2  | 2  |
| Units: nanomole * hour /Liter<br>(nmol*h/L)            |  |  |  |  |
| geometric mean (geometric coefficient<br>of variation) | 31.7 (± 33.4)  | 48.0 (± 26.9)  | 53.3 (± 6.91)  | 138 (± 7.52)   |

| End point values                                       | Phase Ia -<br>Schedule C: BI<br>894999 5/2.5<br>mg (DLBCL<br>patients) | Phase Ib -<br>Schedule B:<br>2.5 mg BI<br>894999 (NC<br>patients) | Phase Ib -<br>Schedule C: BI<br>894999 7/3.5<br>mg (NC<br>patients) | Phase Ib -<br>Schedule B: BI<br>894999 2 mg<br>(solid<br>tumours+NC) |
|--|--|---|---|--|
| Subject group type                                     | Reporting group  | Reporting group   | Subject analysis set  | Subject analysis set   |
| Number of subjects analysed                            | 0 <sup>[47]</sup>  | 17  | 1   | 9  |
| Units: nanomole * hour /Liter<br>(nmol*h/L)            |  |   |   |  |
| geometric mean (geometric coefficient<br>of variation) | ()   | 56.9 (± 58.6)   | 999999 (±<br>999999)  | 39.2 (± 38.8)  |

Notes:

[47] - No subjects in this arm were analyzed for this endpoint.

| End point values                                       | Phase Ib -<br>Schedule B: BI<br>894999 2.5 mg<br>(solid tumours<br>+ NC) | Phase Ib -<br>Schedule C: BI<br>894999 6/3 mg<br>(NC patients) |  |  |
|--|--|--|--|--|
| Subject group type                                     | Subject analysis set   | Subject analysis set   |  |  |
| Number of subjects analysed                            | 42   | 2  |  |  |
| Units: nanomole * hour /Liter<br>(nmol*h/L)            |  |  |  |  |
| geometric mean (geometric coefficient<br>of variation) | 67.6 (± 50.9)  | 214 (± 6.01)   |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Phase Ia and Phase Ib: Maximum measured concentration of BI 894999 in plasma after the first dose (C<sub>max</sub>)

|                 |   |
|-----------------|---|
| End point title | Phase Ia and Phase Ib: Maximum measured concentration of BI 894999 in plasma after the first dose (C <sub>max</sub> ) <sup>[48]</sup> |
|-----------------|---|

End point description:

Maximum measured concentration of BI 894999 in plasma after the first dose (C<sub>max</sub>) for Phase 1a and Phase 1b is reported.

999999=NA- C<sub>max</sub> could not be provided to reduce the risk of patient re-identification.

Pharmacokinetic (PK) analysis Set (PKS): Included all patients in the treated set (TS) who have at least one evaluable PK parameters. Only participants with evaluable results for this PK parameter are reported.

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

End point timeframe:

5 minutes (min) before and at 30 min, 1 hour (h), 2h, 3h, 4h, 6h, 8h and 23h55min after administration of first BI 894999 dose on Day 1 of Cycle 1.

Notes:

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

Justification: In phase Ib, solid tumor patients (SCLC, mCRPC, CRC and NC) are combined by dose level (2 or 2.5mg) as data of all solid tumor patients were needed since no differences were expected, but the NC patients alone were differentiated in an additional subgroup as it was the initial indication for BI 894999.

| End point values                                    | Phase Ia -<br>Schedule A:<br>0.2 mg BI<br>894999 | Phase Ia -<br>Schedule A:<br>0.5 mg BI<br>894999 | Phase Ia -<br>Schedule A: 1<br>mg BI 894999 | Phase Ia -<br>Schedule A:<br>1.5 mg BI<br>894999 |
|---|--|--|---|--|
| Subject group type                                  | Reporting group                                  | Reporting group                                  | Reporting group                             | Reporting group                                  |
| Number of subjects analysed                         | 2  | 2  | 3   | 5  |
| Units: nanomole/L (nmol/L)                          |  |  |   |  |
| geometric mean (geometric coefficient of variation) | 0.393 (± 35.6)                                   | 0.569 (± 46.2)                                   | 1.75 (± 31.6)                               | 3.79 (± 84.0)                                    |

| End point values                                    | Phase Ia -<br>Schedule A: 2<br>mg BI 894999 | Phase Ia -<br>Schedule A: 5<br>mg BI 894999 | Phase Ia -<br>Schedule B:<br>1.5 mg BI<br>894999 | Phase Ia -<br>Schedule B: 2<br>mg BI 894999 |
|---|---|---|--|---|
| Subject group type                                  | Reporting group                             | Reporting group                             | Reporting group                                  | Reporting group                             |
| Number of subjects analysed                         | 4   | 2   | 3  | 4   |
| Units: nanomole/L (nmol/L)                          |   |   |  |   |
| geometric mean (geometric coefficient of variation) | 7.39 (± 56.0)                               | 16.2 (± 68.0)                               | 3.00 (± 155)                                     | 3.93 (± 50.2)                               |

| End point values                                    | Phase Ia -<br>Schedule B:<br>2.5 mg BI<br>894999 | Phase Ia -<br>Schedule C:<br>5/2.5 mg BI<br>894999 | Phase Ia -<br>Schedule C:<br>6/3 mg BI<br>894999 | Phase Ia -<br>Schedule C:<br>7/3.5 mg BI<br>894999 |
|---|--|--|--|--|
| Subject group type                                  | Reporting group                                  | Reporting group                                    | Reporting group                                  | Reporting group                                    |
| Number of subjects analysed                         | 11   | 4  | 15   | 12   |
| Units: nanomole/L (nmol/L)                          |  |  |  |  |
| geometric mean (geometric coefficient of variation) | 4.48 (± 46.6)                                    | 12.0 (± 85.1)                                      | 19.4 (± 58.4)                                    | 21.0 (± 48.3)                                      |

| End point values                                    | Phase Ia -<br>Schedule B:<br>1.5 mg BI<br>894999 (DLBCL<br>patients) | Phase Ia -<br>Schedule B: 2<br>mg BI 894999<br>(DLBCL<br>patients) | Phase Ia -<br>Schedule B:<br>2.5 mg BI<br>894999 (DLBCL<br>patients) | Phase Ia -<br>Schedule C:<br>4/2 mg BI<br>894999 (DLBCL<br>patients) |
|---|--|--|--|--|
| Subject group type                                  | Reporting group  | Reporting group  | Reporting group  | Reporting group  |
| Number of subjects analysed                         | 7  | 4  | 2  | 2  |
| Units: nanomole/L (nmol/L)                          |  |  |  |  |
| geometric mean (geometric coefficient of variation) | 2.98 (± 34.9)  | 4.49 (± 36.0)  | 4.75 (± 0.595)   | 13.9 (± 12.8)  |

| End point values                                    | Phase Ia -<br>Schedule C: BI<br>894999 5/2.5<br>mg (DLBCL<br>patients) | Phase Ib -<br>Schedule B:<br>2.5 mg BI<br>894999 (NC<br>patients) | Phase Ib -<br>Schedule C: BI<br>894999 7/3.5<br>mg (NC<br>patients) | Phase Ib -<br>Schedule B: BI<br>894999 2 mg<br>(solid<br>tumours+NC) |
|---|--|---|---|--|
| Subject group type                                  | Reporting group  | Reporting group   | Subject analysis set  | Subject analysis set   |
| Number of subjects analysed                         | 1  | 17  | 1   | 9  |
| Units: nanomole/L (nmol/L)                          |  |   |   |  |
| geometric mean (geometric coefficient of variation) | 999999 (± 999999)  | 4.88 (± 50.1)   | 999999 (± 999999)   | 4.10 (± 37.8)  |

| End point values                                    | Phase Ib -<br>Schedule B: BI<br>894999 2.5 mg<br>(solid tumours<br>+ NC) | Phase Ib -<br>Schedule C: BI<br>894999 6/3 mg<br>(NC patients) |  |  |
|---|--|--|--|--|
| Subject group type                                  | Subject analysis set   | Subject analysis set   |  |  |
| Number of subjects analysed                         | 44   | 15   |  |  |
| Units: nanomole/L (nmol/L)                          |  |  |  |  |
| geometric mean (geometric coefficient of variation) | 6.01 (± 59.6)  | 18.8 (± 55.8)  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Phase Ia and Phase Ib: Area under the concentration-time curve of BI 894999 in plasma at steady state over a uniform dosing interval $\tau$ (AUC<sub>τ, ss</sub>)

|                 |   |
|-----------------|---|
| End point title | Phase Ia and Phase Ib: Area under the concentration-time curve of BI 894999 in plasma at steady state over a uniform dosing interval $\tau$ (AUC <sub>τ, ss</sub> ) <sup>[49]</sup> |
|-----------------|---|

End point description:

Area under the concentration-time curve of BI 894999 in plasma at steady state over a uniform dosing interval  $\tau$  (AUC<sub>τ, ss</sub>) for Phase Ia and Ib is reported. The dosing interval is 24 hours (h) for all dose groups.

999999=NA-AUC<sub>τ, ss</sub> could not be provided to reduce the risk of patient re-identification.

Pharmacokinetic (PK) analysis Set (PKS): Included all patients in the treated set (TS) who have at least one evaluable PK parameters. Only participants with evaluable results for this PK parameter are reported.

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



End point timeframe:

5 minutes (min) before and at 30 min, 1 hour (h), 2h, 3h, 4h, 6h, 8h, and at 23h55min (Schedule A) or 24h (Schedule B & C) following administration on day 14 (Schedule A & B) or day 21 (Schedule C).

Notes:

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

Justification: In phase Ib, solid tumor patients (SCLC, mCRPC, CRC and NC) are combined by dose level (2 or 2.5mg) as data of all solid tumor patients were needed since no differences were expected, but the NC patients alone were differentiated in an additional subgroup as it was the initial indication for BI 894999.

| End point values                                    | Phase Ia -<br>Schedule A:<br>0.2 mg BI<br>894999 | Phase Ia -<br>Schedule A:<br>0.5 mg BI<br>894999 | Phase Ia -<br>Schedule A: 1<br>mg BI 894999 | Phase Ia -<br>Schedule A:<br>1.5 mg BI<br>894999 |
|---|--|--|---|--|
| Subject group type                                  | Reporting group                                  | Reporting group                                  | Reporting group                             | Reporting group                                  |
| Number of subjects analysed                         | 2  | 2  | 3   | 4  |
| Units: nanomole *hour/Liter (nmol*h/L)              |  |  |   |  |
| geometric mean (geometric coefficient of variation) | 10.3 (± 72.6)                                    | 17.9 (± 46.4)                                    | 54.6 (± 40.4)                               | 76.4 (± 26.6)                                    |

| End point values                                    | Phase Ia -<br>Schedule A: 2<br>mg BI 894999 | Phase Ia -<br>Schedule A: 5<br>mg BI 894999 | Phase Ia -<br>Schedule B:<br>1.5 mg BI<br>894999 | Phase Ia -<br>Schedule B: 2<br>mg BI 894999 |
|---|---|---|--|---|
| Subject group type                                  | Reporting group                             | Reporting group                             | Reporting group                                  | Reporting group                             |
| Number of subjects analysed                         | 4   | 1   | 4  | 6   |
| Units: nanomole *hour/Liter (nmol*h/L)              |   |   |  |   |
| geometric mean (geometric coefficient of variation) | 119 (± 90.3)                                | 999999 (± 999999)                           | 62.6 (± 49.2)                                    | 81.1 (± 32.1)                               |

| End point values                                    | Phase Ia -<br>Schedule B:<br>2.5 mg BI<br>894999 | Phase Ia -<br>Schedule C:<br>5/2.5 mg BI<br>894999 | Phase Ia -<br>Schedule C:<br>6/3 mg BI<br>894999 | Phase Ia -<br>Schedule C:<br>7/3.5 mg BI<br>894999 |
|---|--|--|--|--|
| Subject group type                                  | Reporting group                                  | Reporting group                                    | Reporting group                                  | Reporting group                                    |
| Number of subjects analysed                         | 11   | 3  | 14   | 5  |
| Units: nanomole *hour/Liter (nmol*h/L)              |  |  |  |  |
| geometric mean (geometric coefficient of variation) | 87.0 (± 28.3)                                    | 144 (± 46.4)                                       | 176 (± 37.0)                                     | 226 (± 63.2)                                       |

| End point values                       | Phase Ia -<br>Schedule B:<br>1.5 mg BI<br>894999 (DLBCL<br>patients) | Phase Ia -<br>Schedule B: 2<br>mg BI 894999<br>(DLBCL<br>patients) | Phase Ia -<br>Schedule B:<br>2.5 mg BI<br>894999 (DLBCL<br>patients) | Phase Ia -<br>Schedule C:<br>4/2 mg BI<br>894999 (DLBCL<br>patients) |
|--|--|--|--|--|
| Subject group type                     | Reporting group  | Reporting group  | Reporting group  | Reporting group  |
| Number of subjects analysed            | 6  | 3  | 1  | 1  |
| Units: nanomole *hour/Liter (nmol*h/L) |  |  |  |  |
| geometric mean (geometric coefficient  | 70.3 (± 38.5)  | 120 (± 19.6)   | 999999 (±  | 999999 (±  |

|               |         |         |
|---------------|---------|---------|
| of variation) | 999999) | 999999) |
|---------------|---------|---------|

| End point values                                    | Phase Ia - Schedule C: BI 894999 5/2.5 mg (DLBCL patients) | Phase Ib - Schedule B: 2.5 mg BI 894999 (NC patients) | Phase Ib - Schedule C: BI 894999 7/3.5 mg (NC patients) | Phase Ib - Schedule B: 2 mg BI 894999 (NC patients only) |
|---|--|---|---|--|
| Subject group type                                  | Reporting group  | Reporting group                                       | Subject analysis set                                    | Subject analysis set                                     |
| Number of subjects analysed                         | 1  | 14  | 0 <sup>[50]</sup>                                       | 1  |
| Units: nanomole *hour/Liter (nmol*h/L)              |  |   |   |  |
| geometric mean (geometric coefficient of variation) | 999999 (± 999999)  | 94.9 (± 43.9)   | ()  | 999999 (± 999999)  |

Notes:

[50] - No subjects in this arm were analyzed for this endpoint.

| End point values                                    | Phase Ib - Schedule B: BI 894999 2 mg (solid tumours + NC) | Phase Ib - Schedule B: BI 894999 2.5 mg (solid tumours + NC) | Phase Ib - Schedule C: BI 894999 6/3 mg (NC patients) |  |
|---|--|--|---|--|
| Subject group type                                  | Subject analysis set                                       | Subject analysis set   | Subject analysis set                                  |  |
| Number of subjects analysed                         | 10   | 33   | 11  |  |
| Units: nanomole *hour/Liter (nmol*h/L)              |  |  |   |  |
| geometric mean (geometric coefficient of variation) | 73.6 (± 58.2)  | 125 (± 50.4)   | 149 (± 56.7)  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Phase Ia and Phase Ib: Maximum measured concentration of BI 894999 in plasma at steady state over a uniform dosing interval $\tau$ (C<sub>max</sub>, ss)

|                 |  |
|-----------------|--|
| End point title | Phase Ia and Phase Ib: Maximum measured concentration of BI 894999 in plasma at steady state over a uniform dosing interval $\tau$ (C <sub>max</sub> , ss) <sup>[51]</sup> |
|-----------------|--|

End point description:

Maximum measured concentration of BI 894999 in plasma at steady state over a uniform dosing interval  $\tau$  (C<sub>max</sub>, ss) for Phase Ia and Phase Ib is reported. The dosing interval is 24 hours (h) for all dose groups.

999999=NA-C<sub>max</sub>, ss could not be provided to reduce the risk of patient re-identification.

Pharmacokinetic (PK) analysis Set (PKS): Included all patients in the treated set (TS) who have at least one evaluable PK parameters. Only participants with evaluable results for this PK parameter are reported.

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

End point timeframe:

5 minutes (min) before and at 30 min, 1 hour (h), 2h, 3h, 4h, 6h, 8h, and at 23h55min (Schedule A) or 24h (Schedule B & C) following administration on day 14 (Schedule A & B) or day 21 (Schedule C).

Notes:

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

Justification: In phase Ib, solid tumor patients (SCLC, mCRPC, CRC and NC) are combined by dose level

(2 or 2.5mg) as data of all solid tumor patients were needed since no differences were expected, but the NC patients alone were differentiated in an additional subgroup as it was the initial indication for BI 894999.

| End point values                                       | Phase Ia -<br>Schedule A:<br>0.2 mg BI<br>894999 | Phase Ia -<br>Schedule A:<br>0.5 mg BI<br>894999 | Phase Ia -<br>Schedule A: 1<br>mg BI 894999 | Phase Ia -<br>Schedule A:<br>1.5 mg BI<br>894999 |
|--|--|--|---|--|
| Subject group type                                     | Reporting group                                  | Reporting group                                  | Reporting group                             | Reporting group                                  |
| Number of subjects analysed                            | 2  | 2  | 3   | 6  |
| Units: nanomole/Liter (nmol/L)                         |  |  |   |  |
| geometric mean (geometric coefficient<br>of variation) | 0.697 (± 59.8)                                   | 1.26 (± 24.9)                                    | 4.06 (± 61.7)                               | 5.25 (± 60.1)                                    |

| End point values                                       | Phase Ia -<br>Schedule A: 2<br>mg BI 894999 | Phase Ia -<br>Schedule A: 5<br>mg BI 894999 | Phase Ia -<br>Schedule B:<br>1.5 mg BI<br>894999 | Phase Ia -<br>Schedule B: 2<br>mg BI 894999 |
|--|---|---|--|---|
| Subject group type                                     | Reporting group                             | Reporting group                             | Reporting group                                  | Reporting group                             |
| Number of subjects analysed                            | 6   | 1   | 4  | 6   |
| Units: nanomole/Liter (nmol/L)                         |   |   |  |   |
| geometric mean (geometric coefficient<br>of variation) | 11.6 (± 54.4)                               | 999999 (±<br>999999)                        | 4.75 (± 46.9)                                    | 5.62 (± 27.7)                               |

| End point values                                       | Phase Ia -<br>Schedule B:<br>2.5 mg BI<br>894999 | Phase Ia -<br>Schedule C:<br>5/2.5 mg BI<br>894999 | Phase Ia -<br>Schedule C:<br>6/3 mg BI<br>894999 | Phase Ia -<br>Schedule C:<br>7/3.5 mg BI<br>894999 |
|--|--|--|--|--|
| Subject group type                                     | Reporting group                                  | Reporting group                                    | Reporting group                                  | Reporting group                                    |
| Number of subjects analysed                            | 11   | 3  | 14   | 5  |
| Units: nanomole/Liter (nmol/L)                         |  |  |  |  |
| geometric mean (geometric coefficient<br>of variation) | 6.94 (± 42.0)                                    | 11.4 (± 56.1)                                      | 13.1 (± 41.8)                                    | 17.1 (± 63.6)                                      |

| End point values                                       | Phase Ia -<br>Schedule B:<br>1.5 mg BI<br>894999 (DLBCL<br>patients) | Phase Ia -<br>Schedule B: 2<br>mg BI 894999<br>(DLBCL<br>patients) | Phase Ia -<br>Schedule B:<br>2.5 mg BI<br>894999 (DLBCL<br>patients) | Phase Ia -<br>Schedule C:<br>4/2 mg BI<br>894999 (DLBCL<br>patients) |
|--|--|--|--|--|
| Subject group type                                     | Reporting group  | Reporting group  | Reporting group  | Reporting group  |
| Number of subjects analysed                            | 6  | 3  | 1  | 1  |
| Units: nanomole/Liter (nmol/L)                         |  |  |  |  |
| geometric mean (geometric coefficient<br>of variation) | 5.48 (± 32.7)  | 7.67 (± 8.44)  | 999999 (±<br>999999)   | 999999 (±<br>999999)   |

| End point values | Phase Ia -<br>Schedule C: BI | Phase Ib -<br>Schedule B: | Phase Ib -<br>Schedule C: BI | Phase Ib -<br>Schedule B: 2 |
|------------------|------------------------------|---------------------------|------------------------------|-----------------------------|
|------------------|------------------------------|---------------------------|------------------------------|-----------------------------|

|   | 894999 5/2.5 mg (DLBCL patients) | 2.5 mg BI 894999 (NC patients) | 894999 7/3.5 mg (NC patients) | mg BI 894999 (NC patients only) |
|---|----------------------------------|--------------------------------|-------------------------------|---------------------------------|
| Subject group type                                  | Reporting group                  | Reporting group                | Subject analysis set          | Subject analysis set            |
| Number of subjects analysed                         | 1                                | 14                             | 0 <sup>[52]</sup>             | 1                               |
| Units: nanomole/Liter (nmol/L)                      |                                  |                                |                               |                                 |
| geometric mean (geometric coefficient of variation) | 999999 (± 999999)                | 7.68 (± 45.4)                  | ()                            | 999999 (± 999999)               |

Notes:

[52] - No subjects were analyzed in this arm for this endpoint.

| End point values                                    | Phase Ib - Schedule B: BI 894999 2 mg (solid tumours + NC) | Phase Ib - Schedule B: BI 894999 2.5 mg (solid tumours + NC) | Phase Ib - Schedule C: BI 894999 6/3 mg (NC patients) |  |
|---|--|--|---|--|
| Subject group type                                  | Subject analysis set                                       | Subject analysis set   | Subject analysis set                                  |  |
| Number of subjects analysed                         | 10   | 33   | 11  |  |
| Units: nanomole/Liter (nmol/L)                      |  |  |   |  |
| geometric mean (geometric coefficient of variation) | 6.51 (± 70.0)  | 10.4 (± 59.4)  | 11.2 (± 60.1)   |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Phase Ia and Phase Ib: Objective response (OR)

|  |  |
|--|--|
| End point title  | Phase Ia and Phase Ib: Objective response (OR) |
| End point description:   |  |
| OR was defined as best overall response (BOR) of complete response (CR) or partial response (PR) with tumour assessment during treatment period for each schedule.<br>For DLBCL patients, a minor response according to Response Evaluation Criteria In Lymphoma 2017 (RECIL 2017) was not part of an objective response.<br>BOR was determined from first treatment administration until the earliest of disease progression, death or last evaluable tumour assessment before start of subsequent anticancer therapy, loss to follow-up or withdrawal of consent, according to the following criteria depending on the type of cancer:<br>- solid tumour patients and mCRPC patients with measurable disease: CT and/ or MRI according to RECIST v1.1, every 2 cycles;<br>- mCRPC patients without measurable disease: bone scan and PSA level according to Prostate Cancer Clinical Trials Working Group 3, every 4 cycles;<br>- DLBCL patients:FDG-PET/CT scans according to RECIL 2017; every 2 cycles. |  |
| End point type   | Secondary                                      |
| End point timeframe:   |  |
| Up to 15 months for Phase 1a and up to 28 months for Phase Ib.   |  |

| End point values            | Phase Ia -<br>Schedule A:<br>0.2 mg BI<br>894999 | Phase Ia -<br>Schedule A:<br>0.5 mg BI<br>894999 | Phase Ia -<br>Schedule A: 1<br>mg BI 894999 | Phase Ia -<br>Schedule A:<br>1.5 mg BI<br>894999 |
|-----------------------------|--|--|---|--|
| Subject group type          | Reporting group                                  | Reporting group                                  | Reporting group                             | Reporting group                                  |
| Number of subjects analysed | 2  | 2  | 3   | 6  |
| Units: Participants         | 0  | 1  | 0   | 1  |

| End point values            | Phase Ia -<br>Schedule A: 2<br>mg BI 894999 | Phase Ia -<br>Schedule A: 5<br>mg BI 894999 | Phase Ia -<br>Schedule B:<br>1.5 mg BI<br>894999 | Phase Ia -<br>Schedule B: 2<br>mg BI 894999 |
|-----------------------------|---|---|--|---|
| Subject group type          | Reporting group                             | Reporting group                             | Reporting group                                  | Reporting group                             |
| Number of subjects analysed | 6   | 2   | 6  | 6   |
| Units: Participants         | 0   | 0   | 1  | 0   |

| End point values            | Phase Ia -<br>Schedule B:<br>2.5 mg BI<br>894999 | Phase Ia -<br>Schedule C:<br>5/2.5 mg BI<br>894999 | Phase Ia -<br>Schedule C:<br>6/3 mg BI<br>894999 | Phase Ia -<br>Schedule C:<br>7/3.5 mg BI<br>894999 |
|-----------------------------|--|--|--|--|
| Subject group type          | Reporting group                                  | Reporting group                                    | Reporting group                                  | Reporting group                                    |
| Number of subjects analysed | 13   | 4  | 15   | 12   |
| Units: Participants         | 0  | 0  | 0  | 0  |

| End point values            | Phase Ia -<br>Schedule B:<br>1.5 mg BI<br>894999 (DLBCL<br>patients) | Phase Ia -<br>Schedule B: 2<br>mg BI 894999<br>(DLBCL<br>patients) | Phase Ia -<br>Schedule B:<br>2.5 mg BI<br>894999 (DLBCL<br>patients) | Phase Ia -<br>Schedule C:<br>4/2 mg BI<br>894999 (DLBCL<br>patients) |
|-----------------------------|--|--|--|--|
| Subject group type          | Reporting group  | Reporting group  | Reporting group  | Reporting group  |
| Number of subjects analysed | 8  | 4  | 2  | 2  |
| Units: Participants         | 0  | 1  | 0  | 0  |

| End point values            | Phase Ia -<br>Schedule C: BI<br>894999 5/2.5<br>mg (DLBCL<br>patients) | Phase Ib -<br>Schedule B: 2<br>or 2.5 mg BI<br>894999 (SCLC<br>patients) | Phase Ib -<br>Schedule B:<br>2.5 mg BI<br>894999 (CRC<br>patients) | Phase Ib -<br>Schedule B: 2<br>or 2.5 mg BI<br>894999<br>(mCRPC<br>patients) |
|-----------------------------|--|--|--|--|
| Subject group type          | Reporting group  | Reporting group  | Reporting group  | Reporting group  |
| Number of subjects analysed | 2  | 12   | 14   | 11   |
| Units: Participants         | 0  | 0  | 0  | 1  |

|                             |   |  |  |  |
|-----------------------------|---|--|--|--|
| <b>End point values</b>     | Phase Ib -<br>Schedule B:<br>2.5 mg BI<br>894999 (NC<br>patients) | Phase Ib -<br>Schedule C:<br>6/3 or 7/3.5<br>mg BI 894999<br>(NC patients) |  |  |
| Subject group type          | Reporting group   | Reporting group  |  |  |
| Number of subjects analysed | 20  | 22   |  |  |
| Units: Participants         | 1   | 2  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Phase Ib: Progression-free survival or (PFS) or radiological PFS for mCRPC patients with non-measurable disease by RECIST v1.1

|                 |  |
|-----------------|--|
| End point title | Phase Ib: Progression-free survival or (PFS) or radiological PFS for mCRPC patients with non-measurable disease by RECIST v1.1 <sup>[53]</sup> |
|-----------------|--|

End point description:

Progression-free survival (PFS) was defined as the time from date of start of BI 894999 to the date of objective disease progression ((PD) defined as 20% increase in the sum of the longest diameter of target lesions) or death, whichever is earlier for SCLC patients, CRC patients, mCRPC patients with measurable disease by Response Evaluation Criteria In Solid Tumors Criteria (RECIST v1.1) and NC patients, with tumour assessment every 2 cycles according to RECIST v1.1 during treatment period or Radiological PFS with tumour assessment by bone scan every 4 cycles for mCRPC patients with non-measurable disease by RECIST v1.1.

For patients with 'event' as an outcome for PFS:

- PFS [days] = date of outcome – date of first treatment administration + 1.

For patients with 'censored' as an outcome for PFS:

- PFS (censored) [days] = date of outcome – date of first treatment administration + 1.

The Kaplan-Meier method was used to calculate the estimates.

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

End point timeframe:

Up to 28 months.

Notes:

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

Justification: Endpoint was specified only for metastatic Castration Resistant Prostate Cancer (mCRPC) patients in Phase Ib.

|                                  |  |  |  |   |
|----------------------------------|--|--|--|---|
| <b>End point values</b>          | Phase Ib -<br>Schedule B: 2<br>or 2.5 mg BI<br>894999 (SCLC<br>patients) | Phase Ib -<br>Schedule B:<br>2.5 mg BI<br>894999 (CRC<br>patients) | Phase Ib -<br>Schedule B: 2<br>or 2.5 mg BI<br>894999<br>(mCRPC<br>patients) | Phase Ib -<br>Schedule B:<br>2.5 mg BI<br>894999 (NC<br>patients) |
| Subject group type               | Reporting group  | Reporting group  | Reporting group  | Reporting group   |
| Number of subjects analysed      | 12 <sup>[54]</sup>   | 14 <sup>[55]</sup>   | 11 <sup>[56]</sup>   | 20 <sup>[57]</sup>  |
| Units: Weeks                     |  |  |  |   |
| median (confidence interval 95%) | 5.6 (5.3 to 6.1)   | 5.6 (4.4 to 10.7)  | 11.9 (8.1 to 24.4)   | 6.9 (6.0 to 11.1)   |

Notes:

[54] - Treated Set (TS) in Phase Ib dose expansion (TS PhIb).

[55] - TS PhIb

[56] - TS PhIb

[57] - TS PhIb

|                                  |  |  |  |  |
|----------------------------------|--|--|--|--|
| <b>End point values</b>          | Phase Ib -<br>Schedule C:<br>6/3 or 7/3.5<br>mg BI 894999<br>(NC patients) |  |  |  |
| Subject group type               | Reporting group  |  |  |  |
| Number of subjects analysed      | 22 <sup>[58]</sup>   |  |  |  |
| Units: Weeks                     |  |  |  |  |
| median (confidence interval 95%) | 7.8 (4.0 to<br>13.0)   |  |  |  |

Notes:

[58] - TS PhIb

## Statistical analyses

No statistical analyses for this end point

## Secondary: Phase Ib: Best overall response

|                 |   |
|-----------------|---|
| End point title | Phase Ib: Best overall response <sup>[59]</sup> |
|-----------------|---|

End point description:

Best overall response (BOR) was determined from first treatment administration until the earliest of disease progression, death or last evaluable tumour assessment before start of subsequent anticancer therapy, loss to follow-up or withdrawal of consent, according to the following criteria depending on the type of cancer:

- solid tumour patients and mCRPC patients with measurable disease: Computerized tomography (CT) and/ or magnetic resonance imaging (MRI) according to RECIST v1.1, every 2 cycles;
- mCRPC patients without measurable disease: bone scan and PSA level according to Prostate Cancer Clinical Trials Working Group 3, every 4 cycles.

Treated Set (TS) in Phase Ib dose expansion (TS PhIb): Included all patients in the TS who were treated in Phase Ib.

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

End point timeframe:

Imaging and assessment performed every 2 cycles (solid tumours patients) or 4 cycles (mCRPC patients) for the entire treatment period, up to 28 months.

Notes:

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

Justification: Endpoint was specified only for the participants of the Phase 1b.

|                             |  |  |  |   |
|-----------------------------|--|--|--|---|
| <b>End point values</b>     | Phase Ib -<br>Schedule B: 2<br>or 2.5 mg BI<br>894999 (SCLC<br>patients) | Phase Ib -<br>Schedule B:<br>2.5 mg BI<br>894999 (CRC<br>patients) | Phase Ib -<br>Schedule B: 2<br>or 2.5 mg BI<br>894999<br>(mCRPC<br>patients) | Phase Ib -<br>Schedule B:<br>2.5 mg BI<br>894999 (NC<br>patients) |
| Subject group type          | Reporting group  | Reporting group  | Reporting group  | Reporting group   |
| Number of subjects analysed | 12   | 14   | 11   | 20  |
| Units: Participants         |  |  |  |   |
| Complete response           | 0  | 0  | 0  | 0   |
| Partial response            | 0  | 0  | 1  | 1   |
| Stable disease              | 1  | 2  | 2  | 7   |
| Progressive disease         | 8  | 10   | 4  | 9   |
| Not evaluable               | 3  | 2  | 4  | 3   |

|              |   |   |   |   |
|--------------|---|---|---|---|
| Not assessed | 0 | 0 | 0 | 0 |
|--------------|---|---|---|---|

|                             |  |  |  |  |
|-----------------------------|--|--|--|--|
| <b>End point values</b>     | Phase Ib -<br>Schedule C:<br>6/3 or 7/3.5<br>mg BI 894999<br>(NC patients) |  |  |  |
| Subject group type          | Reporting group  |  |  |  |
| Number of subjects analysed | 22   |  |  |  |
| Units: Participants         |  |  |  |  |
| Complete response           | 1  |  |  |  |
| Partial response            | 1  |  |  |  |
| Stable disease              | 6  |  |  |  |
| Progressive disease         | 9  |  |  |  |
| Not evaluable               | 5  |  |  |  |
| Not assessed                | 0  |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Phase Ib: Overall survival

|                 |  |
|-----------------|--|
| End point title | Phase Ib: Overall survival <sup>[60]</sup> |
|-----------------|--|

End point description:

Overall survival (OS) was defined as the time from first administration of BI 894999 until death from any cause in patients with NUT carcinoma.

For patients with 'event' as an outcome for OS:

- OS [days] = date of outcome – date of first treatment administration + 1.

For patients with 'censored' as an outcome for OS:

- OS (censored) [days] = date of outcome – date of first treatment administration + 1.

The Kaplan-Meier method was used to calculate the estimates.

+(-)999999=NA-Could not be calculated due to low number of participants with missing values.

Patients in NC Schedules B and C in Phase Ib dose expansion and after approval of protocol version 11.0 and gave consent to the collection of overall survival status.

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

End point timeframe:

Up to 28 months.

Notes:

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

Justification: Endpoint was specified only for NUT carcinoma patients in Phase Ib.

|                                  |   |  |  |  |
|----------------------------------|---|--|--|--|
| <b>End point values</b>          | Phase Ib -<br>Schedule B:<br>2.5 mg BI<br>894999 (NC<br>patients) | Phase Ib -<br>Schedule C:<br>6/3 or 7/3.5<br>mg BI 894999<br>(NC patients) |  |  |
| Subject group type               | Reporting group   | Reporting group  |  |  |
| Number of subjects analysed      | 1   | 22   |  |  |
| Units: Weeks                     |   |  |  |  |
| median (confidence interval 95%) | 6.6 (-999999  | 15.4 (7.6 to   |  |  |



## Statistical analyses

No statistical analyses for this end point

### Secondary: Phase Ib: Prostate Specific Antigen (PSA) response in patients with Metastatic Castration Resistant Prostate Cancer (mCRPC)

|                 |   |
|-----------------|---|
| End point title | Phase Ib: Prostate Specific Antigen (PSA) response in patients with Metastatic Castration Resistant Prostate Cancer (mCRPC) <sup>[61]</sup> |
|-----------------|---|

End point description:

PSA response was defined as a decline in PSA value  $\geq 50\%$  from baseline (which is confirmed by a second value 3 to 4 weeks apart).

mCRPC Schedule B in Phase Ib dose expansion (mCRPC): Included all mCRPC patients in the treated set who were treated in Phase Ib with Schedule B.

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

End point timeframe:

Up to 93 days.

Notes:

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

Justification: Endpoint was specified only for metastatic Castration Resistant Prostate Cancer (mCRPC) patients in Phase Ib.

|                             |   |  |  |  |
|-----------------------------|---|--|--|--|
| <b>End point values</b>     | Phase Ib - Schedule B: 2 or 2.5 mg BI 894999 (mCRPC patients) |  |  |  |
| Subject group type          | Reporting group   |  |  |  |
| Number of subjects analysed | 11  |  |  |  |
| Units: Participants         | 0   |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

[Serious and Other Adverse Events]: From first date of dosing of study treatment until date of the last dosing of study treatment + 30 days residual effect period, up to 463 days for Phase 1a and up to 883 days for Phase Ib.

Adverse event reporting additional description:

[All-Cause Mortality]: From first date of dosing until end of study, up to 1309 days for Phase 1a and up to 860 days for Phase Ib.

Treated Set (TS): Included all patients who were dispensed study treatment and were documented to have taken at least one dose of the study treatment.

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

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 24.1 |
|--------------------|------|

### Reporting groups

|                       |   |
|-----------------------|---|
| Reporting group title | Phase Ia - Schedule A: 0.2 mg BI 894999 |
|-----------------------|---|

Reporting group description:

Adult patients with a confirmed diagnosis of advanced, unresectable and/or metastatic malignant solid tumours who had failed conventional treatment or for whom no therapy of proven efficacy existed or who were not amenable to standard therapies were administered orally 0.2 milligram (mg) of BI 894999 once daily, in the morning, after an overnight fast, 1 hour before breakfast with at least 250 milliliter (mL) of water. Schedule A was a continuous daily intake in cycles of 21 days.

|                       |                                       |
|-----------------------|---------------------------------------|
| Reporting group title | Phase Ia - Schedule A: 1 mg BI 894999 |
|-----------------------|---------------------------------------|

Reporting group description:

Adult patients with a confirmed diagnosis of advanced, unresectable and/or metastatic malignant solid tumours who had failed conventional treatment or for whom no therapy of proven efficacy existed or who were not amenable to standard therapies were administered orally 1 milligram (mg) of BI 894999 once daily, in the morning, after an overnight fast, 1 hour before breakfast with at least 250 milliliter (mL) of water. Schedule A was a continuous daily intake in cycles of 21 days.

|                       |   |
|-----------------------|---|
| Reporting group title | Phase Ia - Schedule A: 1.5 mg BI 894999 |
|-----------------------|---|

Reporting group description:

Adult patients with a confirmed diagnosis of advanced, unresectable and/or metastatic malignant solid tumours who had failed conventional treatment or for whom no therapy of proven efficacy existed or who were not amenable to standard therapies were administered orally 1.5 milligram (mg) of BI 894999 once daily, in the morning, after an overnight fast, 1 hour before breakfast with at least 250 milliliter (mL) of water. Schedule A was a continuous daily intake in cycles of 21 days.

|                       |                                       |
|-----------------------|---------------------------------------|
| Reporting group title | Phase Ia - Schedule A: 2 mg BI 894999 |
|-----------------------|---------------------------------------|

Reporting group description:

Adult patients with a confirmed diagnosis of advanced, unresectable and/or metastatic malignant solid tumours who had failed conventional treatment or for whom no therapy of proven efficacy existed or who were not amenable to standard therapies were administered orally 2 milligram (mg) of BI 894999 once daily, in the morning, after an overnight fast, 1 hour before breakfast with at least 250 milliliter (mL) of water. Schedule A was a continuous daily intake in cycles of 21 days.

|                       |   |
|-----------------------|---|
| Reporting group title | Phase Ia - Schedule C: 6/3 mg BI 894999 |
|-----------------------|---|

Reporting group description:

Adult patients with a confirmed diagnosis of advanced, unresectable and/or metastatic malignant solid tumours who had failed conventional treatment or for whom no therapy of proven efficacy existed or who were not amenable to standard therapies were administered orally once daily on Day 1 and on Day 15 of each cycle a loading dose of 6 milligram (mg) of BI 894999, followed by six days daily intake of the maintenance dose of 3 mg of BI 894999 once daily, followed by one week off, repeated every two weeks in cycles of 28 days (Schedule C). The loading and the maintenance dose were administered in the morning, after an overnight fast, 1 hour before breakfast with at least 250 milliliter (mL) of water.

|                       |   |
|-----------------------|---|
| Reporting group title | Phase Ia - Schedule B: 1.5 mg BI 894999 |
|-----------------------|---|

Reporting group description:

Adult patients with a confirmed diagnosis of advanced, unresectable and/or metastatic malignant solid

tumours who had failed conventional treatment or for whom no therapy of proven efficacy existed or who were not amenable to standard therapies were administered orally 1.5 milligram (mg) of BI 894999 once daily, in the morning, after an overnight fast, 1 hour before breakfast with at least 250 milliliter (mL) of water. Schedule B was a continuous intake for 14 days followed by one week off treatment in cycles of 21 days.

|                       |                                       |
|-----------------------|---------------------------------------|
| Reporting group title | Phase Ia - Schedule B: 2 mg BI 894999 |
|-----------------------|---------------------------------------|

Reporting group description:

Adult patients with a confirmed diagnosis of advanced, unresectable and/or metastatic malignant solid tumours who had failed conventional treatment or for whom no therapy of proven efficacy existed or who were not amenable to standard therapies were administered orally 2 milligram (mg) of BI 894999 once daily, in the morning, after an overnight fast, 1 hour before breakfast with at least 250 milliliter (mL) of water. Schedule B was a continuous intake for 14 days followed by one week off treatment in cycles of 21 days.

|                       |   |
|-----------------------|---|
| Reporting group title | Phase Ia - Schedule B: 2.5 mg BI 894999 |
|-----------------------|---|

Reporting group description:

Adult patients with a confirmed diagnosis of advanced, unresectable and/or metastatic malignant solid tumours who had failed conventional treatment or for whom no therapy of proven efficacy existed or who were not amenable to standard therapies were administered orally 2.5 mg of BI 894999 once daily, in the morning, after an overnight fast, 1 hour before breakfast with at least 250 milliliter (mL) of water. Schedule B was a continuous intake for 14 days followed by one week off treatment in cycles of 21 days.

|                       |   |
|-----------------------|---|
| Reporting group title | Phase Ia - Schedule C: 5/2.5 mg BI 894999 |
|-----------------------|---|

Reporting group description:

Adult patients with a confirmed diagnosis of advanced, unresectable and/or metastatic malignant solid tumours who had failed conventional treatment or for whom no therapy of proven efficacy existed or who were not amenable to standard therapies were administered orally once daily on Day 1 and on Day 15 of each cycle a loading dose of 5 milligram (mg) of BI 894999, followed by six days daily intake of the maintenance dose of 2.5 mg of BI 894999 once daily, followed by one week off, repeated every two weeks in cycles of 28 days (Schedule C). The loading and the maintenance dose were administered in the morning, after an overnight fast, 1 hour before breakfast with at least 250 milliliter (mL) of water.

|                       |  |
|-----------------------|--|
| Reporting group title | Phase Ia - Schedule A: 0.5 mg BI 89499 |
|-----------------------|--|

Reporting group description:

Adult patients with a confirmed diagnosis of advanced, unresectable and/or metastatic malignant solid tumours who had failed conventional treatment or for whom no therapy of proven efficacy existed or who were not amenable to standard therapies were administered orally 0.5 milligram (mg) of BI 894999 once daily, in the morning, after an overnight fast, 1 hour before breakfast with at least 250 milliliter (mL) of water. Schedule A was a continuous daily intake in cycles of 21 days.

|                       |                                       |
|-----------------------|---------------------------------------|
| Reporting group title | Phase Ia - Schedule A: 5 mg BI 894999 |
|-----------------------|---------------------------------------|

Reporting group description:

Adult patients with a confirmed diagnosis of advanced, unresectable and/or metastatic malignant solid tumours who had failed conventional treatment or for whom no therapy of proven efficacy existed or who were not amenable to standard therapies were administered orally 5 milligram (mg) of BI 894999 once daily, in the morning, after an overnight fast, 1 hour before breakfast with at least 250 milliliter (mL) of water. Schedule A was a continuous daily intake in cycles of 21 days.

|                       |   |
|-----------------------|---|
| Reporting group title | Phase Ia - Schedule C: 7/3.5 mg BI 894999 |
|-----------------------|---|

Reporting group description:

Adult patients with a confirmed diagnosis of advanced, unresectable and/or metastatic malignant solid tumours who had failed conventional treatment or for whom no therapy of proven efficacy existed or who were not amenable to standard therapies were administered orally once daily on Day 1 and on Day 15 of each cycle a loading dose of 7 milligram (mg) of BI 894999, followed by six days daily intake of the maintenance dose of 3.5 mg of BI 894999 once daily, followed by one week off, repeated every two weeks in cycles of 28 days (Schedule C). The loading and the maintenance dose were administered in the morning, after an overnight fast, 1 hour before breakfast with at least 250 milliliter (mL) of water.

|                       |  |
|-----------------------|--|
| Reporting group title | Phase Ia - Schedule B: 1.5 mg BI 894999 (DLBCL patients) |
|-----------------------|--|

Reporting group description:

Adult patients with histologically confirmed diagnosis of diffuse large B-cell lymphoma (DLBCL) were administered orally 1.5 milligram (mg) of BI 894999 once daily, in the morning, after an overnight fast, 1 hour before breakfast with at least 250 milliliter (mL) of water. Schedule B was a continuous intake for 14 days followed by one week off treatment in cycles of 21 days.

|                       |   |
|-----------------------|---|
| Reporting group title | Phase Ib - Schedule B: 2.5 mg BI 894999 (SCLC patients) |
|-----------------------|---|

Reporting group description:

Adult patients diagnosed with small cell lung cancer (SCLC) were administered 2.5 milligram (mg) of BI 894999 once daily. BI 894999 administration was performed in the morning, after an overnight fast, 1

hour before breakfast with at least 250 milliliter (mL) of water according to Schedule B (continuous intake for 14 days followed by one week off treatment in cycles of 21 days).

|                       |  |
|-----------------------|--|
| Reporting group title | Phase Ia - Schedule C: BI 894999 5/2.5 mg (DLBCL patients) |
|-----------------------|--|

Reporting group description:

Adult patients with histologically confirmed diagnosis of diffuse large B-cell lymphoma (DLBCL) were administered orally once daily on Day 1 and on Day 15 of each cycle a loading dose of 5 milligram (mg) of BI 894999, followed by six days daily intake of the maintenance dose of 2.5 mg of BI 894999, followed by one week off, repeated every two weeks in cycles of 28 days (Schedule C). The loading and the maintenance dose were administered in the morning, after an overnight fast, 1 hour before breakfast with at least 250 milliliter (mL) of water.

|                       |  |
|-----------------------|--|
| Reporting group title | Phase Ia - Schedule C: 4/2 mg BI 894999 (DLBCL patients) |
|-----------------------|--|

Reporting group description:

Adult patients with histologically confirmed diagnosis of diffuse large B-cell lymphoma (DLBCL) were administered orally once daily on Day 1 and on Day 15 of each cycle a loading dose of 4 milligram (mg) of BI 894999, followed by six days daily intake of the maintenance dose of 2 mg of BI 894999 once daily, followed by one week off, repeated every two weeks in cycles of 28 days (Schedule C). The loading and the maintenance dose were administered in the morning, after an overnight fast, 1 hour before breakfast with at least 250 milliliter (mL) of water.

|                       |  |
|-----------------------|--|
| Reporting group title | Phase Ia - Schedule B: 2.5 mg BI 894999 (DLBCL patients) |
|-----------------------|--|

Reporting group description:

Adult patients with histologically confirmed diagnosis of diffuse large B-cell lymphoma (DLBCL) were administered orally 2.5 milligram (mg) of BI 894999 once daily, in the morning, after an overnight fast, 1 hour before breakfast with at least 250 milliliter (mL) of water. Schedule B was a continuous intake for 14 days followed by one week off treatment in cycles of 21 days.

|                       |  |
|-----------------------|--|
| Reporting group title | Phase Ia - Schedule B: 2.5 mg BI 894999 (DLBCL patients) |
|-----------------------|--|

Reporting group description:

Adult patients with histologically confirmed diagnosis of diffuse large B-cell lymphoma (DLBCL) were administered orally 2.5 milligram (mg) of BI 894999 once daily, in the morning, after an overnight fast, 1 hour before breakfast with at least 250 milliliter (mL) of water. Schedule B was a continuous intake for 14 days followed by one week off treatment in cycles of 21 days.

|                       |   |
|-----------------------|---|
| Reporting group title | Phase Ib - Schedule B: 2 mg BI 894999 (SCLC patients) |
|-----------------------|---|

Reporting group description:

Adult patients diagnosed with small cell lung cancer (SCLC) were administered orally 2 milligram (mg) of BI 894999 once daily. BI 894999 administration was performed in the morning, after an overnight fast, 1 hour before breakfast with at least 250 milliliter (mL) of water according to Schedule B (continuous intake for 14 days followed by one week off treatment in cycles of 21 days).

|                       |   |
|-----------------------|---|
| Reporting group title | Phase Ib - Schedule C: BI 894999 6/3 mg (NC patients) |
|-----------------------|---|

Reporting group description:

Adult patients diagnosed with NUT carcinoma (NC) were administered orally once daily on Day 1 and on Day 15 of each cycle a loading dose of 6 milligram (mg) of BI 894999, followed by six days intake of the maintenance dose of 3 mg of BI 894999 once daily, followed by one week off, repeated every two weeks in cycles of 28 days (Schedule C).

|                       |   |
|-----------------------|---|
| Reporting group title | Phase Ib - Schedule B: 2.5 mg BI 894999 (NC patients) |
|-----------------------|---|

Reporting group description:

Adult patients diagnosed with NUT carcinoma (NC) were administered orally 2.5 milligram (mg) of BI 894999 once daily, in the morning, after an overnight fast, 1 hour before breakfast with at least 250 milliliter (mL) of water. Schedule B was a continuous intake for 14 days followed by one week off treatment in cycles of 21 days. The 2.5 mg dose could be reduced to 2 mg in case of adverse events.

|                       |  |
|-----------------------|--|
| Reporting group title | Phase Ib - Schedule B: 2 mg BI 894999 (mCRPC patients) |
|-----------------------|--|

Reporting group description:

Adult patients diagnosed with metastatic castrate resistant prostate cancer (mCRPC) were administered orally 2 milligram (mg) of BI 894999 once daily. BI 894999 administration was performed in the morning, after an overnight fast, 1 hour before breakfast with at least 250 milliliter (mL) of water according to Schedule B (continuous intake for 14 days followed by one week off treatment in cycles of 21 days).

|                       |  |
|-----------------------|--|
| Reporting group title | Phase Ib - Schedule B: 2.5 mg BI 894999 (mCRPC patients) |
|-----------------------|--|

Reporting group description:

Adult patients diagnosed with metastatic castrate resistant prostate cancer (mCRPC) were administered orally 2.5 milligram (mg) of BI 894999 once daily. BI 894999 administration was performed in the morning, after an overnight fast, 1 hour before breakfast with at least 250 milliliter (mL) of water according to Schedule B (continuous intake for 14 days followed by one week off treatment in cycles of

21 days).

|                       |  |
|-----------------------|--|
| Reporting group title | Phase Ib - Schedule B: 2.5 mg BI 894999 (CRC patients) |
|-----------------------|--|

Reporting group description:

Adult patients diagnosed with colorectal cancer (CRC) were administered orally 2.5 milligram (mg) of BI 894999 once daily. BI 894999 administration was performed in the morning, after an overnight fast, 1 hour before breakfast with at least 250 milliliter (mL) of water according to Schedule B (continuous intake for 14 days followed by one week off treatment in cycles of 21 days).

|                       |   |
|-----------------------|---|
| Reporting group title | Phase Ib - Schedule C: BI 894999 7/3.5 mg (NC patients) |
|-----------------------|---|

Reporting group description:

This arm included adult patients diagnosed with NUT carcinoma (NC) who were administered orally once daily on Day 1 and on Day 15 of each cycle a loading dose of 7 milligram (mg) of BI 894999, followed by six days intake of the maintenance dose of 3.5 mg of BI 894999 once daily, followed by one week off, repeated every two weeks in cycles of 28 days (Schedule C). The loading and the maintenance dose were administered in the morning, after an overnight fast, 1 hour before breakfast with at least 250 milliliter (mL) of water.

| Serious adverse events  | Phase Ia - Schedule A: 0.2 mg BI 894999 | Phase Ia - Schedule A: 1 mg BI 894999 | Phase Ia - Schedule A: 1.5 mg BI 894999 |
|---|---|---------------------------------------|---|
| Total subjects affected by serious adverse events                   |   |                                       |   |
| subjects affected / exposed   | 1 / 2 (50.00%)                          | 0 / 3 (0.00%)                         | 3 / 6 (50.00%)                          |
| number of deaths (all causes)                                       | 0                                       | 0                                     | 1                                       |
| number of deaths resulting from adverse events                      | 0                                       | 0                                     | 0                                       |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |   |                                       |   |
| Cancer pain   |   |                                       |   |
| subjects affected / exposed   | 0 / 2 (0.00%)                           | 0 / 3 (0.00%)                         | 0 / 6 (0.00%)                           |
| occurrences causally related to treatment / all                     | 0 / 0                                   | 0 / 0                                 | 0 / 0                                   |
| deaths causally related to treatment / all                          | 0 / 0                                   | 0 / 0                                 | 0 / 0                                   |
| Malignant neoplasm progression                                      |   |                                       |   |
| subjects affected / exposed   | 0 / 2 (0.00%)                           | 0 / 3 (0.00%)                         | 1 / 6 (16.67%)                          |
| occurrences causally related to treatment / all                     | 0 / 0                                   | 0 / 0                                 | 0 / 1                                   |
| deaths causally related to treatment / all                          | 0 / 0                                   | 0 / 0                                 | 0 / 1                                   |
| Metastases to spinal cord   |   |                                       |   |
| subjects affected / exposed   | 0 / 2 (0.00%)                           | 0 / 3 (0.00%)                         | 0 / 6 (0.00%)                           |
| occurrences causally related to treatment / all                     | 0 / 0                                   | 0 / 0                                 | 0 / 0                                   |
| deaths causally related to treatment / all                          | 0 / 0                                   | 0 / 0                                 | 0 / 0                                   |
| Tumour associated fever   |   |                                       |   |
| subjects affected / exposed   | 0 / 2 (0.00%)                           | 0 / 3 (0.00%)                         | 0 / 6 (0.00%)                           |
| occurrences causally related to treatment / all                     | 0 / 0                                   | 0 / 0                                 | 0 / 0                                   |
| deaths causally related to treatment / all                          | 0 / 0                                   | 0 / 0                                 | 0 / 0                                   |
| Tumour haemorrhage  |   |                                       |   |

|   |               |               |               |
|---|---------------|---------------|---------------|
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Tumour pain                                     |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Vascular disorders                              |               |               |               |
| Deep vein thrombosis                            |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Embolism  |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Hypotension                                     |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Jugular vein distension                         |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Vascular occlusion                              |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Surgical and medical procedures                 |               |               |               |
| Euthanasia                                      |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| General disorders and administration            |               |               |               |

|   |               |               |               |
|---|---------------|---------------|---------------|
| site conditions                                 |               |               |               |
| Asthenia  |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Chest pain                                      |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Death   |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Disease progression                             |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Fatigue   |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| General physical health deterioration           |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Non-cardiac chest pain                          |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Pain  |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Pyrexia   |               |               |               |

|   |                |               |               |
|---|----------------|---------------|---------------|
| subjects affected / exposed                     | 0 / 2 (0.00%)  | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Respiratory, thoracic and mediastinal disorders |                |               |               |
| Bronchial obstruction                           |                |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%)  | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Dyspnoea  |                |               |               |
| subjects affected / exposed                     | 1 / 2 (50.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Epistaxis                                       |                |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%)  | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Increased bronchial secretion                   |                |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%)  | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Laryngeal inflammation                          |                |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%)  | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Laryngeal obstruction                           |                |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%)  | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Pleural effusion                                |                |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%)  | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Pneumonitis                                     |                |               |               |



|   |               |               |               |
|---|---------------|---------------|---------------|
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Pneumothorax                                    |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Pulmonary congestion                            |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Pulmonary fistula                               |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Pulmonary haemorrhage                           |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Psychiatric disorders                           |               |               |               |
| Delirium  |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Investigations                                  |               |               |               |
| Blood bilirubin increased                       |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Blood creatine phosphokinase MB increased       |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |

|   |               |               |                |
|---|---------------|---------------|----------------|
| Blood creatine phosphokinase increased          |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Blood creatinine increased                      |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Electrocardiogram QT prolonged                  |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 1 / 6 (16.67%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 1 / 1          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Electrocardiogram ST segment elevation          |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 1 / 6 (16.67%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 1 / 1          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Electrocardiogram T wave inversion              |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Platelet count decreased                        |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Troponin I increased                            |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Troponin T increased                            |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Injury, poisoning and procedural                |               |               |                |

|   |               |               |               |
|---|---------------|---------------|---------------|
| complications                                   |               |               |               |
| Fracture  |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Subdural haematoma                              |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Tendon rupture                                  |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Wound   |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Cardiac disorders                               |               |               |               |
| Acute myocardial infarction                     |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Atrial fibrillation                             |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Cardiac arrest                                  |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Cardiac failure congestive                      |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |

|   |               |               |               |
|---|---------------|---------------|---------------|
| Cardiogenic shock                               |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Pericardial effusion                            |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Supraventricular tachycardia                    |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Nervous system disorders                        |               |               |               |
| Cerebrovascular accident                        |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Headache  |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Ischaemic stroke                                |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Neuralgia                                       |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Seizure   |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Somnolence                                      |               |               |               |

|   |               |               |               |
|---|---------------|---------------|---------------|
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Spinal cord compression                         |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Syncope   |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Blood and lymphatic system disorders            |               |               |               |
| Anaemia   |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Febrile neutropenia                             |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Thrombocytopenia                                |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Eye disorders                                   |               |               |               |
| Eye haemorrhage                                 |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Uveitis   |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Gastrointestinal disorders                      |               |               |               |

|   |               |               |                |
|---|---------------|---------------|----------------|
| Abdominal pain                                  |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 1 / 6 (16.67%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Abdominal pain upper                            |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Diarrhoea                                       |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Duodenal ulcer                                  |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Gastrointestinal haemorrhage                    |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Lower gastrointestinal haemorrhage              |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Nausea  |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Oral pain                                       |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Small intestinal haemorrhage                    |               |               |                |

|   |               |               |               |
|---|---------------|---------------|---------------|
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Small intestinal obstruction                    |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Upper gastrointestinal haemorrhage              |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Vomiting  |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Hepatobiliary disorders                         |               |               |               |
| Biliary obstruction                             |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Cholangitis                                     |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Skin and subcutaneous tissue disorders          |               |               |               |
| Dermatitis acneiform                            |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Pruritus  |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Skin necrosis                                   |               |               |               |

|   |               |               |               |
|---|---------------|---------------|---------------|
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Renal and urinary disorders                     |               |               |               |
| Acute kidney injury                             |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Bladder dilatation                              |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Calculus urinary                                |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Haematuria                                      |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Urinary retention                               |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Musculoskeletal and connective tissue disorders |               |               |               |
| Arthralgia                                      |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Osteonecrosis of jaw                            |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |



|   |               |               |               |
|---|---------------|---------------|---------------|
| Pain in extremity                               |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Pain in jaw                                     |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Infections and infestations                     |               |               |               |
| Abdominal infection                             |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Bronchitis                                      |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| COVID-19  |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Cystitis  |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Dacryocystitis                                  |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Device related infection                        |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Hepatic infection                               |               |               |               |

|   |               |               |                |
|---|---------------|---------------|----------------|
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Infection                                       |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Influenza                                       |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 1 / 6 (16.67%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Localised infection                             |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Lower respiratory tract infection               |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Meningitis pneumococcal                         |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Periorbital cellulitis                          |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Pneumonia                                       |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Pneumonia aspiration                            |               |               |                |

|   |               |               |               |
|---|---------------|---------------|---------------|
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Sepsis  |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Spinal cord infection                           |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Urinary tract infection                         |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Metabolism and nutrition disorders              |               |               |               |
| Dehydration                                     |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Hypercalcaemia                                  |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Hyperglycaemia                                  |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Hypokalaemia                                    |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Hyponatraemia                                   |               |               |               |

|   |               |               |               |
|---|---------------|---------------|---------------|
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Hypophosphataemia                               |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |

| <b>Serious adverse events</b>                                       | Phase Ia - Schedule A: 2 mg BI 894999 | Phase Ia - Schedule C: 6/3 mg BI 894999 | Phase Ia - Schedule B: 1.5 mg BI 894999 |
|---|---------------------------------------|---|---|
| Total subjects affected by serious adverse events                   |                                       |   |   |
| subjects affected / exposed   | 2 / 6 (33.33%)                        | 8 / 15 (53.33%)                         | 3 / 6 (50.00%)                          |
| number of deaths (all causes)                                       | 1                                     | 2                                       | 1                                       |
| number of deaths resulting from adverse events                      | 1                                     | 0                                       | 0                                       |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                                       |   |   |
| Cancer pain   |                                       |   |   |
| subjects affected / exposed   | 0 / 6 (0.00%)                         | 0 / 15 (0.00%)                          | 0 / 6 (0.00%)                           |
| occurrences causally related to treatment / all                     | 0 / 0                                 | 0 / 0                                   | 0 / 0                                   |
| deaths causally related to treatment / all                          | 0 / 0                                 | 0 / 0                                   | 0 / 0                                   |
| Malignant neoplasm progression                                      |                                       |   |   |
| subjects affected / exposed   | 0 / 6 (0.00%)                         | 0 / 15 (0.00%)                          | 1 / 6 (16.67%)                          |
| occurrences causally related to treatment / all                     | 0 / 0                                 | 0 / 0                                   | 0 / 1                                   |
| deaths causally related to treatment / all                          | 0 / 0                                 | 0 / 0                                   | 0 / 1                                   |
| Metastases to spinal cord   |                                       |   |   |
| subjects affected / exposed   | 0 / 6 (0.00%)                         | 0 / 15 (0.00%)                          | 0 / 6 (0.00%)                           |
| occurrences causally related to treatment / all                     | 0 / 0                                 | 0 / 0                                   | 0 / 0                                   |
| deaths causally related to treatment / all                          | 0 / 0                                 | 0 / 0                                   | 0 / 0                                   |
| Tumour associated fever   |                                       |   |   |
| subjects affected / exposed   | 0 / 6 (0.00%)                         | 0 / 15 (0.00%)                          | 0 / 6 (0.00%)                           |
| occurrences causally related to treatment / all                     | 0 / 0                                 | 0 / 0                                   | 0 / 0                                   |
| deaths causally related to treatment / all                          | 0 / 0                                 | 0 / 0                                   | 0 / 0                                   |
| Tumour haemorrhage  |                                       |   |   |

|   |               |                |               |
|---|---------------|----------------|---------------|
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Tumour pain                                     |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 1 / 15 (6.67%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 2          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Vascular disorders                              |               |                |               |
| Deep vein thrombosis                            |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Embolism  |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Hypotension                                     |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Jugular vein distension                         |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Vascular occlusion                              |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Surgical and medical procedures                 |               |                |               |
| Euthanasia                                      |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| General disorders and administration            |               |                |               |

|   |               |                |                |
|---|---------------|----------------|----------------|
| site conditions                                 |               |                |                |
| Asthenia  |               |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Chest pain                                      |               |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Death   |               |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Disease progression                             |               |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Fatigue   |               |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| General physical health deterioration           |               |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Non-cardiac chest pain                          |               |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 1 / 6 (16.67%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Pain  |               |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Pyrexia   |               |                |                |

|   |               |                |               |
|---|---------------|----------------|---------------|
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Respiratory, thoracic and mediastinal disorders |               |                |               |
| Bronchial obstruction                           |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Dyspnoea  |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 1 / 15 (6.67%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 1          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 1          | 0 / 0         |
| Epistaxis                                       |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Increased bronchial secretion                   |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Laryngeal inflammation                          |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Laryngeal obstruction                           |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Pleural effusion                                |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Pneumonitis                                     |               |                |               |

|   |               |                |               |
|---|---------------|----------------|---------------|
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Pneumothorax                                    |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Pulmonary congestion                            |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Pulmonary fistula                               |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Pulmonary haemorrhage                           |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Psychiatric disorders                           |               |                |               |
| Delirium  |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Investigations                                  |               |                |               |
| Blood bilirubin increased                       |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Blood creatine phosphokinase MB increased       |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 1 / 15 (6.67%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 1 / 1          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |



|   |                |                 |               |  |
|---|----------------|-----------------|---------------|--|
| Blood creatine phosphokinase increased          |                |                 |               |  |
| subjects affected / exposed                     | 1 / 6 (16.67%) | 1 / 15 (6.67%)  | 0 / 6 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1          | 1 / 1           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0         |  |
| Blood creatinine increased                      |                |                 |               |  |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  | 0 / 6 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0         |  |
| Electrocardiogram QT prolonged                  |                |                 |               |  |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  | 0 / 6 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0         |  |
| Electrocardiogram ST segment elevation          |                |                 |               |  |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  | 0 / 6 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0         |  |
| Electrocardiogram T wave inversion              |                |                 |               |  |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  | 0 / 6 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0         |  |
| Platelet count decreased                        |                |                 |               |  |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  | 0 / 6 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0         |  |
| Troponin I increased                            |                |                 |               |  |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  | 0 / 6 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0         |  |
| Troponin T increased                            |                |                 |               |  |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 2 / 15 (13.33%) | 0 / 6 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 2 / 2           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0         |  |
| Injury, poisoning and procedural                |                |                 |               |  |

|   |               |                |               |
|---|---------------|----------------|---------------|
| complications                                   |               |                |               |
| Fracture  |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Subdural haematoma                              |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Tendon rupture                                  |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Wound   |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Cardiac disorders                               |               |                |               |
| Acute myocardial infarction                     |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Atrial fibrillation                             |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Cardiac arrest                                  |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Cardiac failure congestive                      |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |

|   |                |                |               |
|---|----------------|----------------|---------------|
| Cardiogenic shock                               |                |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Pericardial effusion                            |                |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Supraventricular tachycardia                    |                |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Nervous system disorders                        |                |                |               |
| Cerebrovascular accident                        |                |                |               |
| subjects affected / exposed                     | 1 / 6 (16.67%) | 0 / 15 (0.00%) | 0 / 6 (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         |
| Headache  |                |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Ischaemic stroke                                |                |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Neuralgia                                       |                |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Seizure   |                |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Somnolence                                      |                |                |               |

|   |               |                |               |
|---|---------------|----------------|---------------|
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Spinal cord compression                         |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Syncope   |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Blood and lymphatic system disorders            |               |                |               |
| Anaemia   |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Febrile neutropenia                             |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Thrombocytopenia                                |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Eye disorders                                   |               |                |               |
| Eye haemorrhage                                 |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Uveitis   |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Gastrointestinal disorders                      |               |                |               |

|   |               |                |                |
|---|---------------|----------------|----------------|
| Abdominal pain                                  |               |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 1 / 15 (6.67%) | 0 / 6 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Abdominal pain upper                            |               |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 1 / 6 (16.67%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Diarrhoea                                       |               |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Duodenal ulcer                                  |               |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Gastrointestinal haemorrhage                    |               |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Lower gastrointestinal haemorrhage              |               |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Nausea  |               |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Oral pain                                       |               |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 1 / 15 (6.67%) | 0 / 6 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Small intestinal haemorrhage                    |               |                |                |

|   |               |                |               |
|---|---------------|----------------|---------------|
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Small intestinal obstruction                    |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Upper gastrointestinal haemorrhage              |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Vomiting  |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Hepatobiliary disorders                         |               |                |               |
| Biliary obstruction                             |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 1 / 15 (6.67%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 1          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Cholangitis                                     |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 1 / 15 (6.67%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 1          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Skin and subcutaneous tissue disorders          |               |                |               |
| Dermatitis acneiform                            |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Pruritus  |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Skin necrosis                                   |               |                |               |

|   |               |                |               |
|---|---------------|----------------|---------------|
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Renal and urinary disorders                     |               |                |               |
| Acute kidney injury                             |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Bladder dilatation                              |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Calculus urinary                                |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Haematuria                                      |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Urinary retention                               |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Musculoskeletal and connective tissue disorders |               |                |               |
| Arthralgia                                      |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 1 / 15 (6.67%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 2          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Osteonecrosis of jaw                            |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |

|   |               |                |               |
|---|---------------|----------------|---------------|
| Pain in extremity                               |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Pain in jaw                                     |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Infections and infestations                     |               |                |               |
| Abdominal infection                             |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 1 / 15 (6.67%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 1          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 1          | 0 / 0         |
| Bronchitis                                      |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| COVID-19  |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Cystitis  |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Dacryocystitis                                  |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Device related infection                        |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Hepatic infection                               |               |                |               |



|   |                |                |               |
|---|----------------|----------------|---------------|
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Infection                                       |                |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Influenza                                       |                |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Localised infection                             |                |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 1 / 15 (6.67%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Lower respiratory tract infection               |                |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Meningitis pneumococcal                         |                |                |               |
| subjects affected / exposed                     | 1 / 6 (16.67%) | 0 / 15 (0.00%) | 0 / 6 (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         |
| Periorbital cellulitis                          |                |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Pneumonia                                       |                |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Pneumonia aspiration                            |                |                |               |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 15 (0.00%) | 0 / 6 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Sepsis  |                |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 15 (0.00%) | 1 / 6 (16.67%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Spinal cord infection                           |                |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 15 (0.00%) | 0 / 6 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Urinary tract infection                         |                |                |                |
| subjects affected / exposed                     | 1 / 6 (16.67%) | 0 / 15 (0.00%) | 0 / 6 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Metabolism and nutrition disorders              |                |                |                |
| Dehydration                                     |                |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 15 (0.00%) | 0 / 6 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Hypercalcaemia                                  |                |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 15 (0.00%) | 0 / 6 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Hyperglycaemia                                  |                |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 15 (0.00%) | 0 / 6 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Hypokalaemia                                    |                |                |                |
| subjects affected / exposed                     | 1 / 6 (16.67%) | 0 / 15 (0.00%) | 0 / 6 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Hyponatraemia                                   |                |                |                |

|   |               |                |                |
|---|---------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Hypophosphataemia                               |               |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 1 / 6 (16.67%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 1 / 1          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |

| <b>Serious adverse events</b>                                       | Phase Ia - Schedule B: 2 mg BI 894999 | Phase Ia - Schedule B: 2.5 mg BI 894999 | Phase Ia - Schedule C: 5/2.5 mg BI 894999 |
|---|---------------------------------------|---|---|
| Total subjects affected by serious adverse events                   |                                       |   |   |
| subjects affected / exposed   | 3 / 6 (50.00%)                        | 6 / 13 (46.15%)                         | 2 / 4 (50.00%)                            |
| number of deaths (all causes)                                       | 1                                     | 2                                       | 0   |
| number of deaths resulting from adverse events                      | 0                                     | 0                                       | 0   |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                                       |   |   |
| Cancer pain   |                                       |   |   |
| subjects affected / exposed   | 0 / 6 (0.00%)                         | 0 / 13 (0.00%)                          | 0 / 4 (0.00%)                             |
| occurrences causally related to treatment / all                     | 0 / 0                                 | 0 / 0                                   | 0 / 0                                     |
| deaths causally related to treatment / all                          | 0 / 0                                 | 0 / 0                                   | 0 / 0                                     |
| Malignant neoplasm progression                                      |                                       |   |   |
| subjects affected / exposed   | 0 / 6 (0.00%)                         | 0 / 13 (0.00%)                          | 0 / 4 (0.00%)                             |
| occurrences causally related to treatment / all                     | 0 / 0                                 | 0 / 0                                   | 0 / 0                                     |
| deaths causally related to treatment / all                          | 0 / 0                                 | 0 / 0                                   | 0 / 0                                     |
| Metastases to spinal cord   |                                       |   |   |
| subjects affected / exposed   | 0 / 6 (0.00%)                         | 1 / 13 (7.69%)                          | 0 / 4 (0.00%)                             |
| occurrences causally related to treatment / all                     | 0 / 0                                 | 0 / 1                                   | 0 / 0                                     |
| deaths causally related to treatment / all                          | 0 / 0                                 | 0 / 0                                   | 0 / 0                                     |
| Tumour associated fever   |                                       |   |   |
| subjects affected / exposed   | 0 / 6 (0.00%)                         | 0 / 13 (0.00%)                          | 0 / 4 (0.00%)                             |
| occurrences causally related to treatment / all                     | 0 / 0                                 | 0 / 0                                   | 0 / 0                                     |
| deaths causally related to treatment / all                          | 0 / 0                                 | 0 / 0                                   | 0 / 0                                     |
| Tumour haemorrhage  |                                       |   |   |

|   |               |                |               |
|---|---------------|----------------|---------------|
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 13 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Tumour pain                                     |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 13 (0.00%) | 0 / 4 (0.00%) |
| 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                              |               |                |               |
| Deep vein thrombosis                            |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 13 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Embolism  |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 13 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Hypotension                                     |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 13 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Jugular vein distension                         |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 13 (0.00%) | 0 / 4 (0.00%) |
| 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 occlusion                              |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 13 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Surgical and medical procedures                 |               |                |               |
| Euthanasia                                      |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 13 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| General disorders and administration            |               |                |               |

|   |               |                |               |
|---|---------------|----------------|---------------|
| site conditions                                 |               |                |               |
| Asthenia  |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 13 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Chest pain                                      |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 13 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Death   |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 13 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Disease progression                             |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 1 / 13 (7.69%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 1          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 1          | 0 / 0         |
| Fatigue   |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 13 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| General physical health deterioration           |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 13 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Non-cardiac chest pain                          |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 13 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Pain  |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 13 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Pyrexia   |               |                |               |

|   |                |                |               |
|---|----------------|----------------|---------------|
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 13 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Respiratory, thoracic and mediastinal disorders |                |                |               |
| Bronchial obstruction                           |                |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 13 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Dyspnoea  |                |                |               |
| subjects affected / exposed                     | 1 / 6 (16.67%) | 0 / 13 (0.00%) | 0 / 4 (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         |
| Epistaxis                                       |                |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 1 / 13 (7.69%) | 0 / 4 (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         |
| Increased bronchial secretion                   |                |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 13 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Laryngeal inflammation                          |                |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 13 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Laryngeal obstruction                           |                |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 13 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Pleural effusion                                |                |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 13 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Pneumonitis                                     |                |                |               |

|   |               |                |                |
|---|---------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 13 (0.00%) | 1 / 4 (25.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Pneumothorax                                    |               |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 13 (0.00%) | 0 / 4 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Pulmonary congestion                            |               |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 13 (0.00%) | 0 / 4 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Pulmonary fistula                               |               |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 13 (0.00%) | 0 / 4 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Pulmonary haemorrhage                           |               |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 13 (0.00%) | 0 / 4 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Psychiatric disorders                           |               |                |                |
| Delirium  |               |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 13 (0.00%) | 0 / 4 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Investigations                                  |               |                |                |
| Blood bilirubin increased                       |               |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 1 / 13 (7.69%) | 0 / 4 (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          |
| Blood creatine phosphokinase MB increased       |               |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 13 (0.00%) | 0 / 4 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |

|   |               |                |               |
|---|---------------|----------------|---------------|
| Blood creatine phosphokinase increased          |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 13 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Blood creatinine increased                      |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 13 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Electrocardiogram QT prolonged                  |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 13 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Electrocardiogram ST segment elevation          |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 13 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Electrocardiogram T wave inversion              |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 13 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Platelet count decreased                        |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 13 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Troponin I increased                            |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 13 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Troponin T increased                            |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 1 / 13 (7.69%) | 0 / 4 (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         |
| Injury, poisoning and procedural                |               |                |               |



|   |               |                |                |
|---|---------------|----------------|----------------|
| complications                                   |               |                |                |
| Fracture  |               |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 13 (0.00%) | 0 / 4 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Subdural haematoma                              |               |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 13 (0.00%) | 0 / 4 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Tendon rupture                                  |               |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 13 (0.00%) | 0 / 4 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Wound   |               |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 13 (0.00%) | 0 / 4 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Cardiac disorders                               |               |                |                |
| Acute myocardial infarction                     |               |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 13 (0.00%) | 1 / 4 (25.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Atrial fibrillation                             |               |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 13 (0.00%) | 0 / 4 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Cardiac arrest                                  |               |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 1 / 13 (7.69%) | 0 / 4 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 1          | 0 / 0          |
| Cardiac failure congestive                      |               |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 13 (0.00%) | 0 / 4 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |

|   |               |                |               |
|---|---------------|----------------|---------------|
| Cardiogenic shock                               |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 13 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Pericardial effusion                            |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 13 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Supraventricular tachycardia                    |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 13 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Nervous system disorders                        |               |                |               |
| Cerebrovascular accident                        |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 13 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Headache  |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 13 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Ischaemic stroke                                |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 13 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Neuralgia                                       |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 13 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Seizure   |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 13 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Somnolence                                      |               |                |               |

|   |               |                |               |
|---|---------------|----------------|---------------|
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 13 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Spinal cord compression                         |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 13 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Syncope   |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 13 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Blood and lymphatic system disorders            |               |                |               |
| Anaemia   |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 13 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Febrile neutropenia                             |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 13 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Thrombocytopenia                                |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 13 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Eye disorders                                   |               |                |               |
| Eye haemorrhage                                 |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 13 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Uveitis   |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 13 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Gastrointestinal disorders                      |               |                |               |

|   |                |                |               |
|---|----------------|----------------|---------------|
| Abdominal pain                                  |                |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 13 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Abdominal pain upper                            |                |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 13 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Diarrhoea                                       |                |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 13 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Duodenal ulcer                                  |                |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 1 / 13 (7.69%) | 0 / 4 (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 haemorrhage                    |                |                |               |
| subjects affected / exposed                     | 1 / 6 (16.67%) | 0 / 13 (0.00%) | 0 / 4 (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         |
| Lower gastrointestinal haemorrhage              |                |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 13 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Nausea  |                |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 13 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Oral pain                                       |                |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 13 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Small intestinal haemorrhage                    |                |                |               |

|   |                |                |               |
|---|----------------|----------------|---------------|
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 1 / 13 (7.69%) | 0 / 4 (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         |
| Small intestinal obstruction                    |                |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 13 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Upper gastrointestinal haemorrhage              |                |                |               |
| subjects affected / exposed                     | 1 / 6 (16.67%) | 0 / 13 (0.00%) | 0 / 4 (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         |
| Vomiting  |                |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 13 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Hepatobiliary disorders                         |                |                |               |
| Biliary obstruction                             |                |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 13 (0.00%) | 0 / 4 (0.00%) |
| 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 / 6 (0.00%)  | 0 / 13 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Skin and subcutaneous tissue disorders          |                |                |               |
| Dermatitis acneiform                            |                |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 13 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Pruritus  |                |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 13 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Skin necrosis                                   |                |                |               |

|   |               |                |               |
|---|---------------|----------------|---------------|
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 13 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Renal and urinary disorders                     |               |                |               |
| Acute kidney injury                             |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 13 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Bladder dilatation                              |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 13 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Calculus urinary                                |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 13 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Haematuria                                      |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 13 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Urinary retention                               |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 13 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Musculoskeletal and connective tissue disorders |               |                |               |
| Arthralgia                                      |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 13 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Osteonecrosis of jaw                            |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 1 / 13 (7.69%) | 0 / 4 (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         |

|   |                |                |                |
|---|----------------|----------------|----------------|
| Pain in extremity                               |                |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 13 (0.00%) | 0 / 4 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Pain in jaw                                     |                |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 13 (0.00%) | 0 / 4 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Infections and infestations                     |                |                |                |
| Abdominal infection                             |                |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 13 (0.00%) | 0 / 4 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Bronchitis                                      |                |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 13 (0.00%) | 0 / 4 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| COVID-19  |                |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 13 (0.00%) | 0 / 4 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Cystitis  |                |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 13 (0.00%) | 1 / 4 (25.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Dacryocystitis                                  |                |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 13 (0.00%) | 0 / 4 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Device related infection                        |                |                |                |
| subjects affected / exposed                     | 1 / 6 (16.67%) | 0 / 13 (0.00%) | 0 / 4 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Hepatic infection                               |                |                |                |

|   |               |                |               |
|---|---------------|----------------|---------------|
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 13 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Infection                                       |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 13 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Influenza                                       |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 13 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Localised infection                             |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 13 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Lower respiratory tract infection               |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 13 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Meningitis pneumococcal                         |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 13 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Periorbital cellulitis                          |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 13 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Pneumonia                                       |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 13 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Pneumonia aspiration                            |               |                |               |



|   |               |                |               |
|---|---------------|----------------|---------------|
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 13 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Sepsis  |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 13 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Spinal cord infection                           |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 1 / 13 (7.69%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 1          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Urinary tract infection                         |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 13 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Metabolism and nutrition disorders              |               |                |               |
| Dehydration                                     |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 13 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Hypercalcaemia                                  |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 13 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Hyperglycaemia                                  |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 13 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Hypokalaemia                                    |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 13 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Hyponatraemia                                   |               |                |               |

|   |               |                |               |
|---|---------------|----------------|---------------|
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 13 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Hypophosphataemia                               |               |                |               |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 13 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |

| <b>Serious adverse events</b>                                       | Phase Ia - Schedule A: 0.5 mg BI 894999 | Phase Ia - Schedule A: 5 mg BI 894999 | Phase Ia - Schedule C: 7/3.5 mg BI 894999 |
|---|---|---------------------------------------|---|
| Total subjects affected by serious adverse events                   |   |                                       |   |
| subjects affected / exposed   | 2 / 2 (100.00%)                         | 1 / 2 (50.00%)                        | 8 / 12 (66.67%)                           |
| number of deaths (all causes)                                       | 0                                       | 0                                     | 1   |
| number of deaths resulting from adverse events                      | 0                                       | 0                                     | 0   |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |   |                                       |   |
| Cancer pain   |   |                                       |   |
| subjects affected / exposed   | 0 / 2 (0.00%)                           | 0 / 2 (0.00%)                         | 1 / 12 (8.33%)                            |
| occurrences causally related to treatment / all                     | 0 / 0                                   | 0 / 0                                 | 0 / 1                                     |
| deaths causally related to treatment / all                          | 0 / 0                                   | 0 / 0                                 | 0 / 0                                     |
| Malignant neoplasm progression                                      |   |                                       |   |
| subjects affected / exposed   | 0 / 2 (0.00%)                           | 0 / 2 (0.00%)                         | 0 / 12 (0.00%)                            |
| occurrences causally related to treatment / all                     | 0 / 0                                   | 0 / 0                                 | 0 / 0                                     |
| deaths causally related to treatment / all                          | 0 / 0                                   | 0 / 0                                 | 0 / 0                                     |
| Metastases to spinal cord   |   |                                       |   |
| subjects affected / exposed   | 0 / 2 (0.00%)                           | 0 / 2 (0.00%)                         | 0 / 12 (0.00%)                            |
| occurrences causally related to treatment / all                     | 0 / 0                                   | 0 / 0                                 | 0 / 0                                     |
| deaths causally related to treatment / all                          | 0 / 0                                   | 0 / 0                                 | 0 / 0                                     |
| Tumour associated fever   |   |                                       |   |
| subjects affected / exposed   | 0 / 2 (0.00%)                           | 0 / 2 (0.00%)                         | 0 / 12 (0.00%)                            |
| occurrences causally related to treatment / all                     | 0 / 0                                   | 0 / 0                                 | 0 / 0                                     |
| deaths causally related to treatment / all                          | 0 / 0                                   | 0 / 0                                 | 0 / 0                                     |
| Tumour haemorrhage  |   |                                       |   |

|   |               |               |                |
|---|---------------|---------------|----------------|
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Tumour pain                                     |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 12 (0.00%) |
| 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                              |               |               |                |
| Deep vein thrombosis                            |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Embolism  |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Hypotension                                     |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Jugular vein distension                         |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 12 (0.00%) |
| 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 occlusion                              |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Surgical and medical procedures                 |               |               |                |
| Euthanasia                                      |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| General disorders and administration            |               |               |                |

|   |                |               |                |
|---|----------------|---------------|----------------|
| site conditions                                 |                |               |                |
| Asthenia  |                |               |                |
| subjects affected / exposed                     | 1 / 2 (50.00%) | 0 / 2 (0.00%) | 0 / 12 (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          |
| Chest pain                                      |                |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0          |
| Death   |                |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0          |
| Disease progression                             |                |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 1 / 12 (8.33%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 1          |
| Fatigue   |                |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 1 / 12 (8.33%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 1 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0          |
| General physical health deterioration           |                |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 1 / 12 (8.33%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0          |
| Non-cardiac chest pain                          |                |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0          |
| Pain  |                |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0          |
| Pyrexia   |                |               |                |

|   |               |                |                |
|---|---------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 2 (0.00%) | 1 / 2 (50.00%) | 0 / 12 (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 |               |                |                |
| Bronchial obstruction                           |               |                |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Dyspnoea  |               |                |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Epistaxis                                       |               |                |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Increased bronchial secretion                   |               |                |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Laryngeal inflammation                          |               |                |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Laryngeal obstruction                           |               |                |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Pleural effusion                                |               |                |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Pneumonitis                                     |               |                |                |

|   |               |               |                |
|---|---------------|---------------|----------------|
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Pneumothorax                                    |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 1 / 12 (8.33%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Pulmonary congestion                            |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Pulmonary fistula                               |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Pulmonary haemorrhage                           |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Psychiatric disorders                           |               |               |                |
| Delirium  |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Investigations                                  |               |               |                |
| Blood bilirubin increased                       |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Blood creatine phosphokinase MB increased       |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |

|   |               |               |                |
|---|---------------|---------------|----------------|
| Blood creatine phosphokinase increased          |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Blood creatinine increased                      |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Electrocardiogram QT prolonged                  |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Electrocardiogram ST segment elevation          |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Electrocardiogram T wave inversion              |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Platelet count decreased                        |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Troponin I increased                            |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Troponin T increased                            |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 1 / 12 (8.33%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 1 / 1          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Injury, poisoning and procedural                |               |               |                |

|   |               |               |                |
|---|---------------|---------------|----------------|
| complications                                   |               |               |                |
| Fracture  |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Subdural haematoma                              |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Tendon rupture                                  |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Wound   |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 1 / 12 (8.33%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Cardiac disorders                               |               |               |                |
| Acute myocardial infarction                     |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Atrial fibrillation                             |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Cardiac arrest                                  |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Cardiac failure congestive                      |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |



|   |                |               |                |
|---|----------------|---------------|----------------|
| Cardiogenic shock                               |                |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0          |
| Pericardial effusion                            |                |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0          |
| Supraventricular tachycardia                    |                |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0          |
| Nervous system disorders                        |                |               |                |
| Cerebrovascular accident                        |                |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0          |
| Headache  |                |               |                |
| subjects affected / exposed                     | 1 / 2 (50.00%) | 0 / 2 (0.00%) | 0 / 12 (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          |
| Ischaemic stroke                                |                |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0          |
| Neuralgia                                       |                |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0          |
| Seizure   |                |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0          |
| Somnolence                                      |                |               |                |

|   |               |                |                 |
|---|---------------|----------------|-----------------|
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 0 / 12 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0           |
| Spinal cord compression                         |               |                |                 |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 0 / 12 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0           |
| Syncope   |               |                |                 |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 1 / 2 (50.00%) | 0 / 12 (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           |
| Blood and lymphatic system disorders            |               |                |                 |
| Anaemia   |               |                |                 |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 2 / 12 (16.67%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 2           |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0           |
| Febrile neutropenia                             |               |                |                 |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 0 / 12 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0           |
| Thrombocytopenia                                |               |                |                 |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 1 / 12 (8.33%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 2 / 2           |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0           |
| Eye disorders                                   |               |                |                 |
| Eye haemorrhage                                 |               |                |                 |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 0 / 12 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0           |
| Uveitis   |               |                |                 |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 0 / 12 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0           |
| Gastrointestinal disorders                      |               |                |                 |

|   |               |               |                |
|---|---------------|---------------|----------------|
| Abdominal pain                                  |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 1 / 12 (8.33%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Abdominal pain upper                            |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Diarrhoea                                       |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 1 / 12 (8.33%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 1 / 1          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Duodenal ulcer                                  |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Gastrointestinal haemorrhage                    |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 1 / 12 (8.33%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Lower gastrointestinal haemorrhage              |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Nausea  |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Oral pain                                       |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Small intestinal haemorrhage                    |               |               |                |

|   |               |               |                |
|---|---------------|---------------|----------------|
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Small intestinal obstruction                    |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Upper gastrointestinal haemorrhage              |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Vomiting  |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Hepatobiliary disorders                         |               |               |                |
| Biliary obstruction                             |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 12 (0.00%) |
| 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 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Skin and subcutaneous tissue disorders          |               |               |                |
| Dermatitis acneiform                            |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Pruritus  |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Skin necrosis                                   |               |               |                |

|   |               |               |                |
|---|---------------|---------------|----------------|
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 1 / 12 (8.33%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Renal and urinary disorders                     |               |               |                |
| Acute kidney injury                             |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 1 / 12 (8.33%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Bladder dilatation                              |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Calculus urinary                                |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Haematuria                                      |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 1 / 12 (8.33%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Urinary retention                               |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Musculoskeletal and connective tissue disorders |               |               |                |
| Arthralgia                                      |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Osteonecrosis of jaw                            |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |

|   |               |               |                |
|---|---------------|---------------|----------------|
| Pain in extremity                               |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Pain in jaw                                     |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Infections and infestations                     |               |               |                |
| Abdominal infection                             |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Bronchitis                                      |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| COVID-19  |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Cystitis  |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Dacryocystitis                                  |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Device related infection                        |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Hepatic infection                               |               |               |                |

|   |               |               |                |
|---|---------------|---------------|----------------|
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Infection                                       |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 1 / 12 (8.33%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Influenza                                       |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Localised infection                             |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Lower respiratory tract infection               |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Meningitis pneumococcal                         |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Periorbital cellulitis                          |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Pneumonia                                       |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Pneumonia aspiration                            |               |               |                |

|   |               |                |                |
|---|---------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Sepsis  |               |                |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Spinal cord infection                           |               |                |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Urinary tract infection                         |               |                |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 1 / 12 (8.33%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Metabolism and nutrition disorders              |               |                |                |
| Dehydration                                     |               |                |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 1 / 2 (50.00%) | 0 / 12 (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          |
| Hypercalcaemia                                  |               |                |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Hyperglycaemia                                  |               |                |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Hypokalaemia                                    |               |                |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 1 / 12 (8.33%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Hyponatraemia                                   |               |                |                |



|   |               |               |                |
|---|---------------|---------------|----------------|
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |
| Hypophosphataemia                               |               |               |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 12 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0          |

| <b>Serious adverse events</b>                                       | Phase Ia - Schedule B: 1.5 mg BI 894999 (DLBCL patients) | Phase Ib - Schedule B: 2.5 mg BI 894999 (SCLC patients) | Phase Ia - Schedule C: BI 894999 5/2.5 mg (DLBCL patients) |
|---|--|---|--|
| Total subjects affected by serious adverse events                   |  |   |  |
| subjects affected / exposed   | 3 / 8 (37.50%)   | 2 / 3 (66.67%)  | 0 / 2 (0.00%)  |
| number of deaths (all causes)                                       | 0  | 0   | 0  |
| number of deaths resulting from adverse events                      | 0  | 0   | 0  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |  |   |  |
| Cancer pain   |  |   |  |
| subjects affected / exposed   | 0 / 8 (0.00%)  | 0 / 3 (0.00%)   | 0 / 2 (0.00%)  |
| occurrences causally related to treatment / all                     | 0 / 0  | 0 / 0   | 0 / 0  |
| deaths causally related to treatment / all                          | 0 / 0  | 0 / 0   | 0 / 0  |
| Malignant neoplasm progression                                      |  |   |  |
| subjects affected / exposed   | 0 / 8 (0.00%)  | 0 / 3 (0.00%)   | 0 / 2 (0.00%)  |
| occurrences causally related to treatment / all                     | 0 / 0  | 0 / 0   | 0 / 0  |
| deaths causally related to treatment / all                          | 0 / 0  | 0 / 0   | 0 / 0  |
| Metastases to spinal cord   |  |   |  |
| subjects affected / exposed   | 0 / 8 (0.00%)  | 0 / 3 (0.00%)   | 0 / 2 (0.00%)  |
| occurrences causally related to treatment / all                     | 0 / 0  | 0 / 0   | 0 / 0  |
| deaths causally related to treatment / all                          | 0 / 0  | 0 / 0   | 0 / 0  |
| Tumour associated fever   |  |   |  |
| subjects affected / exposed   | 0 / 8 (0.00%)  | 0 / 3 (0.00%)   | 0 / 2 (0.00%)  |
| occurrences causally related to treatment / all                     | 0 / 0  | 0 / 0   | 0 / 0  |
| deaths causally related to treatment / all                          | 0 / 0  | 0 / 0   | 0 / 0  |
| Tumour haemorrhage  |  |   |  |

|   |               |               |               |
|---|---------------|---------------|---------------|
| subjects affected / exposed                     | 0 / 8 (0.00%) | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Tumour pain                                     |               |               |               |
| subjects affected / exposed                     | 0 / 8 (0.00%) | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| 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                              |               |               |               |
| Deep vein thrombosis                            |               |               |               |
| subjects affected / exposed                     | 0 / 8 (0.00%) | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Embolism  |               |               |               |
| subjects affected / exposed                     | 0 / 8 (0.00%) | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Hypotension                                     |               |               |               |
| subjects affected / exposed                     | 0 / 8 (0.00%) | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Jugular vein distension                         |               |               |               |
| subjects affected / exposed                     | 0 / 8 (0.00%) | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| 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 occlusion                              |               |               |               |
| subjects affected / exposed                     | 0 / 8 (0.00%) | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Surgical and medical procedures                 |               |               |               |
| Euthanasia                                      |               |               |               |
| subjects affected / exposed                     | 0 / 8 (0.00%) | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| General disorders and administration            |               |               |               |

|   |               |               |               |
|---|---------------|---------------|---------------|
| site conditions                                 |               |               |               |
| Asthenia  |               |               |               |
| subjects affected / exposed                     | 0 / 8 (0.00%) | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Chest pain                                      |               |               |               |
| subjects affected / exposed                     | 0 / 8 (0.00%) | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Death   |               |               |               |
| subjects affected / exposed                     | 0 / 8 (0.00%) | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Disease progression                             |               |               |               |
| subjects affected / exposed                     | 0 / 8 (0.00%) | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Fatigue   |               |               |               |
| subjects affected / exposed                     | 0 / 8 (0.00%) | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| General physical health deterioration           |               |               |               |
| subjects affected / exposed                     | 0 / 8 (0.00%) | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Non-cardiac chest pain                          |               |               |               |
| subjects affected / exposed                     | 0 / 8 (0.00%) | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Pain  |               |               |               |
| subjects affected / exposed                     | 0 / 8 (0.00%) | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Pyrexia   |               |               |               |

|   |               |                |               |
|---|---------------|----------------|---------------|
| subjects affected / exposed                     | 0 / 8 (0.00%) | 0 / 3 (0.00%)  | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Respiratory, thoracic and mediastinal disorders |               |                |               |
| Bronchial obstruction                           |               |                |               |
| subjects affected / exposed                     | 0 / 8 (0.00%) | 0 / 3 (0.00%)  | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Dyspnoea  |               |                |               |
| subjects affected / exposed                     | 0 / 8 (0.00%) | 0 / 3 (0.00%)  | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Epistaxis                                       |               |                |               |
| subjects affected / exposed                     | 0 / 8 (0.00%) | 0 / 3 (0.00%)  | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Increased bronchial secretion                   |               |                |               |
| subjects affected / exposed                     | 0 / 8 (0.00%) | 0 / 3 (0.00%)  | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Laryngeal inflammation                          |               |                |               |
| subjects affected / exposed                     | 0 / 8 (0.00%) | 1 / 3 (33.33%) | 0 / 2 (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         |
| Laryngeal obstruction                           |               |                |               |
| subjects affected / exposed                     | 0 / 8 (0.00%) | 0 / 3 (0.00%)  | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Pleural effusion                                |               |                |               |
| subjects affected / exposed                     | 0 / 8 (0.00%) | 0 / 3 (0.00%)  | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Pneumonitis                                     |               |                |               |

|   |               |               |               |
|---|---------------|---------------|---------------|
| subjects affected / exposed                     | 0 / 8 (0.00%) | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Pneumothorax                                    |               |               |               |
| subjects affected / exposed                     | 0 / 8 (0.00%) | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Pulmonary congestion                            |               |               |               |
| subjects affected / exposed                     | 0 / 8 (0.00%) | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Pulmonary fistula                               |               |               |               |
| subjects affected / exposed                     | 0 / 8 (0.00%) | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Pulmonary haemorrhage                           |               |               |               |
| subjects affected / exposed                     | 0 / 8 (0.00%) | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Psychiatric disorders                           |               |               |               |
| Delirium  |               |               |               |
| subjects affected / exposed                     | 0 / 8 (0.00%) | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Investigations                                  |               |               |               |
| Blood bilirubin increased                       |               |               |               |
| subjects affected / exposed                     | 0 / 8 (0.00%) | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Blood creatine phosphokinase MB increased       |               |               |               |
| subjects affected / exposed                     | 0 / 8 (0.00%) | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |

|   |                |                |               |
|---|----------------|----------------|---------------|
| Blood creatine phosphokinase increased          |                |                |               |
| subjects affected / exposed                     | 0 / 8 (0.00%)  | 0 / 3 (0.00%)  | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Blood creatinine increased                      |                |                |               |
| subjects affected / exposed                     | 1 / 8 (12.50%) | 0 / 3 (0.00%)  | 0 / 2 (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         |
| Electrocardiogram QT prolonged                  |                |                |               |
| subjects affected / exposed                     | 0 / 8 (0.00%)  | 0 / 3 (0.00%)  | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Electrocardiogram ST segment elevation          |                |                |               |
| subjects affected / exposed                     | 0 / 8 (0.00%)  | 0 / 3 (0.00%)  | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Electrocardiogram T wave inversion              |                |                |               |
| subjects affected / exposed                     | 0 / 8 (0.00%)  | 1 / 3 (33.33%) | 0 / 2 (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         |
| Platelet count decreased                        |                |                |               |
| subjects affected / exposed                     | 0 / 8 (0.00%)  | 0 / 3 (0.00%)  | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Troponin I increased                            |                |                |               |
| subjects affected / exposed                     | 0 / 8 (0.00%)  | 0 / 3 (0.00%)  | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Troponin T increased                            |                |                |               |
| subjects affected / exposed                     | 0 / 8 (0.00%)  | 0 / 3 (0.00%)  | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Injury, poisoning and procedural                |                |                |               |

|   |               |               |               |
|---|---------------|---------------|---------------|
| complications                                   |               |               |               |
| Fracture  |               |               |               |
| subjects affected / exposed                     | 0 / 8 (0.00%) | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Subdural haematoma                              |               |               |               |
| subjects affected / exposed                     | 0 / 8 (0.00%) | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Tendon rupture                                  |               |               |               |
| subjects affected / exposed                     | 0 / 8 (0.00%) | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Wound   |               |               |               |
| subjects affected / exposed                     | 0 / 8 (0.00%) | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Cardiac disorders                               |               |               |               |
| Acute myocardial infarction                     |               |               |               |
| subjects affected / exposed                     | 0 / 8 (0.00%) | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Atrial fibrillation                             |               |               |               |
| subjects affected / exposed                     | 0 / 8 (0.00%) | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Cardiac arrest                                  |               |               |               |
| subjects affected / exposed                     | 0 / 8 (0.00%) | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Cardiac failure congestive                      |               |               |               |
| subjects affected / exposed                     | 0 / 8 (0.00%) | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |

|   |               |               |               |
|---|---------------|---------------|---------------|
| Cardiogenic shock                               |               |               |               |
| subjects affected / exposed                     | 0 / 8 (0.00%) | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Pericardial effusion                            |               |               |               |
| subjects affected / exposed                     | 0 / 8 (0.00%) | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Supraventricular tachycardia                    |               |               |               |
| subjects affected / exposed                     | 0 / 8 (0.00%) | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Nervous system disorders                        |               |               |               |
| Cerebrovascular accident                        |               |               |               |
| subjects affected / exposed                     | 0 / 8 (0.00%) | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Headache  |               |               |               |
| subjects affected / exposed                     | 0 / 8 (0.00%) | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Ischaemic stroke                                |               |               |               |
| subjects affected / exposed                     | 0 / 8 (0.00%) | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Neuralgia                                       |               |               |               |
| subjects affected / exposed                     | 0 / 8 (0.00%) | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Seizure   |               |               |               |
| subjects affected / exposed                     | 0 / 8 (0.00%) | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Somnolence                                      |               |               |               |



|   |                |                |               |
|---|----------------|----------------|---------------|
| subjects affected / exposed                     | 0 / 8 (0.00%)  | 0 / 3 (0.00%)  | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Spinal cord compression                         |                |                |               |
| subjects affected / exposed                     | 0 / 8 (0.00%)  | 0 / 3 (0.00%)  | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Syncope   |                |                |               |
| subjects affected / exposed                     | 0 / 8 (0.00%)  | 0 / 3 (0.00%)  | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Blood and lymphatic system disorders            |                |                |               |
| Anaemia   |                |                |               |
| subjects affected / exposed                     | 1 / 8 (12.50%) | 0 / 3 (0.00%)  | 0 / 2 (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         |
| Febrile neutropenia                             |                |                |               |
| subjects affected / exposed                     | 0 / 8 (0.00%)  | 0 / 3 (0.00%)  | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Thrombocytopenia                                |                |                |               |
| subjects affected / exposed                     | 0 / 8 (0.00%)  | 2 / 3 (66.67%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 3 / 3          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Eye disorders                                   |                |                |               |
| Eye haemorrhage                                 |                |                |               |
| subjects affected / exposed                     | 0 / 8 (0.00%)  | 0 / 3 (0.00%)  | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Uveitis   |                |                |               |
| subjects affected / exposed                     | 0 / 8 (0.00%)  | 0 / 3 (0.00%)  | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0         |
| Gastrointestinal disorders                      |                |                |               |

|   |               |               |               |
|---|---------------|---------------|---------------|
| Abdominal pain                                  |               |               |               |
| subjects affected / exposed                     | 0 / 8 (0.00%) | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Abdominal pain upper                            |               |               |               |
| subjects affected / exposed                     | 0 / 8 (0.00%) | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Diarrhoea                                       |               |               |               |
| subjects affected / exposed                     | 0 / 8 (0.00%) | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Duodenal ulcer                                  |               |               |               |
| subjects affected / exposed                     | 0 / 8 (0.00%) | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Gastrointestinal haemorrhage                    |               |               |               |
| subjects affected / exposed                     | 0 / 8 (0.00%) | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Lower gastrointestinal haemorrhage              |               |               |               |
| subjects affected / exposed                     | 0 / 8 (0.00%) | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Nausea  |               |               |               |
| subjects affected / exposed                     | 0 / 8 (0.00%) | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Oral pain                                       |               |               |               |
| subjects affected / exposed                     | 0 / 8 (0.00%) | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Small intestinal haemorrhage                    |               |               |               |

|   |               |               |               |
|---|---------------|---------------|---------------|
| subjects affected / exposed                     | 0 / 8 (0.00%) | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Small intestinal obstruction                    |               |               |               |
| subjects affected / exposed                     | 0 / 8 (0.00%) | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Upper gastrointestinal haemorrhage              |               |               |               |
| subjects affected / exposed                     | 0 / 8 (0.00%) | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Vomiting  |               |               |               |
| subjects affected / exposed                     | 0 / 8 (0.00%) | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Hepatobiliary disorders                         |               |               |               |
| Biliary obstruction                             |               |               |               |
| subjects affected / exposed                     | 0 / 8 (0.00%) | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| 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 / 8 (0.00%) | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Skin and subcutaneous tissue disorders          |               |               |               |
| Dermatitis acneiform                            |               |               |               |
| subjects affected / exposed                     | 0 / 8 (0.00%) | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Pruritus  |               |               |               |
| subjects affected / exposed                     | 0 / 8 (0.00%) | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Skin necrosis                                   |               |               |               |

|   |               |               |               |
|---|---------------|---------------|---------------|
| subjects affected / exposed                     | 0 / 8 (0.00%) | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Renal and urinary disorders                     |               |               |               |
| Acute kidney injury                             |               |               |               |
| subjects affected / exposed                     | 0 / 8 (0.00%) | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Bladder dilatation                              |               |               |               |
| subjects affected / exposed                     | 0 / 8 (0.00%) | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Calculus urinary                                |               |               |               |
| subjects affected / exposed                     | 0 / 8 (0.00%) | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Haematuria                                      |               |               |               |
| subjects affected / exposed                     | 0 / 8 (0.00%) | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Urinary retention                               |               |               |               |
| subjects affected / exposed                     | 0 / 8 (0.00%) | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Musculoskeletal and connective tissue disorders |               |               |               |
| Arthralgia                                      |               |               |               |
| subjects affected / exposed                     | 0 / 8 (0.00%) | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Osteonecrosis of jaw                            |               |               |               |
| subjects affected / exposed                     | 0 / 8 (0.00%) | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |

|   |                |               |               |
|---|----------------|---------------|---------------|
| Pain in extremity                               |                |               |               |
| subjects affected / exposed                     | 1 / 8 (12.50%) | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Pain in jaw                                     |                |               |               |
| subjects affected / exposed                     | 0 / 8 (0.00%)  | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Infections and infestations                     |                |               |               |
| Abdominal infection                             |                |               |               |
| subjects affected / exposed                     | 0 / 8 (0.00%)  | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Bronchitis                                      |                |               |               |
| subjects affected / exposed                     | 1 / 8 (12.50%) | 0 / 3 (0.00%) | 0 / 2 (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         |
| COVID-19  |                |               |               |
| subjects affected / exposed                     | 0 / 8 (0.00%)  | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Cystitis  |                |               |               |
| subjects affected / exposed                     | 0 / 8 (0.00%)  | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Dacryocystitis                                  |                |               |               |
| subjects affected / exposed                     | 0 / 8 (0.00%)  | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Device related infection                        |                |               |               |
| subjects affected / exposed                     | 0 / 8 (0.00%)  | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Hepatic infection                               |                |               |               |

|   |                |               |               |
|---|----------------|---------------|---------------|
| subjects affected / exposed                     | 0 / 8 (0.00%)  | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Infection                                       |                |               |               |
| subjects affected / exposed                     | 0 / 8 (0.00%)  | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Influenza                                       |                |               |               |
| subjects affected / exposed                     | 0 / 8 (0.00%)  | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Localised infection                             |                |               |               |
| subjects affected / exposed                     | 0 / 8 (0.00%)  | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Lower respiratory tract infection               |                |               |               |
| subjects affected / exposed                     | 0 / 8 (0.00%)  | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Meningitis pneumococcal                         |                |               |               |
| subjects affected / exposed                     | 0 / 8 (0.00%)  | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Periorbital cellulitis                          |                |               |               |
| subjects affected / exposed                     | 0 / 8 (0.00%)  | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Pneumonia                                       |                |               |               |
| subjects affected / exposed                     | 1 / 8 (12.50%) | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Pneumonia aspiration                            |                |               |               |

|   |               |               |               |
|---|---------------|---------------|---------------|
| subjects affected / exposed                     | 0 / 8 (0.00%) | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Sepsis  |               |               |               |
| subjects affected / exposed                     | 0 / 8 (0.00%) | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Spinal cord infection                           |               |               |               |
| subjects affected / exposed                     | 0 / 8 (0.00%) | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Urinary tract infection                         |               |               |               |
| subjects affected / exposed                     | 0 / 8 (0.00%) | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Metabolism and nutrition disorders              |               |               |               |
| Dehydration                                     |               |               |               |
| subjects affected / exposed                     | 0 / 8 (0.00%) | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Hypercalcaemia                                  |               |               |               |
| subjects affected / exposed                     | 0 / 8 (0.00%) | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Hyperglycaemia                                  |               |               |               |
| subjects affected / exposed                     | 0 / 8 (0.00%) | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Hypokalaemia                                    |               |               |               |
| subjects affected / exposed                     | 0 / 8 (0.00%) | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Hyponatraemia                                   |               |               |               |

|   |               |               |               |
|---|---------------|---------------|---------------|
| subjects affected / exposed                     | 0 / 8 (0.00%) | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Hypophosphataemia                               |               |               |               |
| subjects affected / exposed                     | 0 / 8 (0.00%) | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |

| <b>Serious adverse events</b>                                       | Phase Ia - Schedule C: 4/2 mg BI 894999 (DLBCL patients) | Phase Ia - Schedule B: 2.5 mg BI 894999 (DLBCL patients) | Phase Ia - Schedule B: 2.5 mg BI 894999 (DLBCL patients) |
|---|--|--|--|
| Total subjects affected by serious adverse events                   |  |  |  |
| subjects affected / exposed   | 1 / 2 (50.00%)   | 2 / 2 (100.00%)  | 2 / 4 (50.00%)   |
| number of deaths (all causes)                                       | 1  | 0  | 0  |
| number of deaths resulting from adverse events                      | 0  | 0  | 0  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |  |  |  |
| Cancer pain   |  |  |  |
| subjects affected / exposed   | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences causally related to treatment / all                     | 0 / 0  | 0 / 0  | 0 / 0  |
| deaths causally related to treatment / all                          | 0 / 0  | 0 / 0  | 0 / 0  |
| Malignant neoplasm progression                                      |  |  |  |
| subjects affected / exposed   | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences causally related to treatment / all                     | 0 / 0  | 0 / 0  | 0 / 0  |
| deaths causally related to treatment / all                          | 0 / 0  | 0 / 0  | 0 / 0  |
| Metastases to spinal cord   |  |  |  |
| subjects affected / exposed   | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences causally related to treatment / all                     | 0 / 0  | 0 / 0  | 0 / 0  |
| deaths causally related to treatment / all                          | 0 / 0  | 0 / 0  | 0 / 0  |
| Tumour associated fever   |  |  |  |
| subjects affected / exposed   | 1 / 2 (50.00%)   | 0 / 2 (0.00%)  | 0 / 4 (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  |
| Tumour haemorrhage  |  |  |  |



|   |                |               |               |
|---|----------------|---------------|---------------|
| subjects affected / exposed                     | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Tumour pain                                     |                |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| 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                              |                |               |               |
| Deep vein thrombosis                            |                |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Embolism  |                |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Hypotension                                     |                |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Jugular vein distension                         |                |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| 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 occlusion                              |                |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Surgical and medical procedures                 |                |               |               |
| Euthanasia                                      |                |               |               |
| subjects affected / exposed                     | 1 / 2 (50.00%) | 0 / 2 (0.00%) | 0 / 4 (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         |
| General disorders and administration            |                |               |               |

|   |                |               |               |  |
|---|----------------|---------------|---------------|--|
| site conditions                                 |                |               |               |  |
| Asthenia  |                |               |               |  |
| subjects affected / exposed                     | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 4 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |  |
| Chest pain                                      |                |               |               |  |
| subjects affected / exposed                     | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 4 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |  |
| Death   |                |               |               |  |
| subjects affected / exposed                     | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 4 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |  |
| Disease progression                             |                |               |               |  |
| subjects affected / exposed                     | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 4 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |  |
| Fatigue   |                |               |               |  |
| subjects affected / exposed                     | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 4 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |  |
| General physical health deterioration           |                |               |               |  |
| subjects affected / exposed                     | 1 / 2 (50.00%) | 0 / 2 (0.00%) | 0 / 4 (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         |  |
| Non-cardiac chest pain                          |                |               |               |  |
| subjects affected / exposed                     | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 4 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |  |
| Pain  |                |               |               |  |
| subjects affected / exposed                     | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 4 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |  |
| Pyrexia   |                |               |               |  |

|   |               |                |               |
|---|---------------|----------------|---------------|
| subjects affected / exposed                     | 0 / 2 (0.00%) | 1 / 2 (50.00%) | 0 / 4 (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 |               |                |               |
| Bronchial obstruction                           |               |                |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Dyspnoea  |               |                |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Epistaxis                                       |               |                |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Increased bronchial secretion                   |               |                |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Laryngeal inflammation                          |               |                |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Laryngeal obstruction                           |               |                |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Pleural effusion                                |               |                |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Pneumonitis                                     |               |                |               |

|   |               |               |               |
|---|---------------|---------------|---------------|
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Pneumothorax                                    |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Pulmonary congestion                            |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Pulmonary fistula                               |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Pulmonary haemorrhage                           |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Psychiatric disorders                           |               |               |               |
| Delirium  |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Investigations                                  |               |               |               |
| Blood bilirubin increased                       |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Blood creatine phosphokinase MB increased       |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |

|   |               |               |               |
|---|---------------|---------------|---------------|
| Blood creatine phosphokinase increased          |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Blood creatinine increased                      |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Electrocardiogram QT prolonged                  |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Electrocardiogram ST segment elevation          |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Electrocardiogram T wave inversion              |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Platelet count decreased                        |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Troponin I increased                            |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Troponin T increased                            |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Injury, poisoning and procedural                |               |               |               |

|   |               |               |               |
|---|---------------|---------------|---------------|
| complications                                   |               |               |               |
| Fracture  |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Subdural haematoma                              |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Tendon rupture                                  |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Wound   |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Cardiac disorders                               |               |               |               |
| Acute myocardial infarction                     |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Atrial fibrillation                             |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Cardiac arrest                                  |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Cardiac failure congestive                      |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |

|   |               |               |               |
|---|---------------|---------------|---------------|
| Cardiogenic shock                               |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Pericardial effusion                            |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Supraventricular tachycardia                    |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Nervous system disorders                        |               |               |               |
| Cerebrovascular accident                        |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Headache  |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Ischaemic stroke                                |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Neuralgia                                       |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Seizure   |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Somnolence                                      |               |               |               |

|   |               |                |                |
|---|---------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Spinal cord compression                         |               |                |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Syncope   |               |                |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Blood and lymphatic system disorders            |               |                |                |
| Anaemia   |               |                |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 1 / 4 (25.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 1 / 1          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Febrile neutropenia                             |               |                |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 1 / 2 (50.00%) | 0 / 4 (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          |
| Thrombocytopenia                                |               |                |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Eye disorders                                   |               |                |                |
| Eye haemorrhage                                 |               |                |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Uveitis   |               |                |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 1 / 4 (25.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Gastrointestinal disorders                      |               |                |                |



|   |               |               |               |
|---|---------------|---------------|---------------|
| Abdominal pain                                  |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Abdominal pain upper                            |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Diarrhoea                                       |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Duodenal ulcer                                  |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Gastrointestinal haemorrhage                    |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Lower gastrointestinal haemorrhage              |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Nausea  |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Oral pain                                       |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Small intestinal haemorrhage                    |               |               |               |

|   |               |               |               |
|---|---------------|---------------|---------------|
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Small intestinal obstruction                    |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Upper gastrointestinal haemorrhage              |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Vomiting  |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Hepatobiliary disorders                         |               |               |               |
| Biliary obstruction                             |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| 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 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Skin and subcutaneous tissue disorders          |               |               |               |
| Dermatitis acneiform                            |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Pruritus  |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Skin necrosis                                   |               |               |               |

|   |               |                |               |
|---|---------------|----------------|---------------|
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Renal and urinary disorders                     |               |                |               |
| Acute kidney injury                             |               |                |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Bladder dilatation                              |               |                |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Calculus urinary                                |               |                |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Haematuria                                      |               |                |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 1 / 2 (50.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 1          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Urinary retention                               |               |                |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Musculoskeletal and connective tissue disorders |               |                |               |
| Arthralgia                                      |               |                |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Osteonecrosis of jaw                            |               |                |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |

|   |               |               |               |
|---|---------------|---------------|---------------|
| Pain in extremity                               |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Pain in jaw                                     |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Infections and infestations                     |               |               |               |
| Abdominal infection                             |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Bronchitis                                      |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| COVID-19  |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Cystitis  |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Dacryocystitis                                  |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Device related infection                        |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Hepatic infection                               |               |               |               |

|   |               |               |               |
|---|---------------|---------------|---------------|
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Infection                                       |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Influenza                                       |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Localised infection                             |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Lower respiratory tract infection               |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Meningitis pneumococcal                         |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Periorbital cellulitis                          |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Pneumonia                                       |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Pneumonia aspiration                            |               |               |               |

|   |               |                |               |
|---|---------------|----------------|---------------|
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Sepsis  |               |                |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 1 / 2 (50.00%) | 0 / 4 (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         |
| Spinal cord infection                           |               |                |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Urinary tract infection                         |               |                |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Metabolism and nutrition disorders              |               |                |               |
| Dehydration                                     |               |                |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Hypercalcaemia                                  |               |                |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Hyperglycaemia                                  |               |                |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Hypokalaemia                                    |               |                |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0         |
| Hyponatraemia                                   |               |                |               |

|   |               |               |               |
|---|---------------|---------------|---------------|
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Hypophosphataemia                               |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |

| <b>Serious adverse events</b>                                       | Phase Ib - Schedule B: 2 mg BI 894999 (SCLC patients) | Phase Ib - Schedule C: BI 894999 6/3 mg (NC patients) | Phase Ib - Schedule B: 2.5 mg BI 894999 (NC patients) |
|---|---|---|---|
| Total subjects affected by serious adverse events                   |   |   |   |
| subjects affected / exposed   | 3 / 9 (33.33%)  | 12 / 21 (57.14%)                                      | 15 / 20 (75.00%)                                      |
| number of deaths (all causes)                                       | 1   | 2   | 5   |
| number of deaths resulting from adverse events                      | 0   | 0   | 0   |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |   |   |   |
| Cancer pain   |   |   |   |
| subjects affected / exposed   | 0 / 9 (0.00%)   | 0 / 21 (0.00%)  | 3 / 20 (15.00%)                                       |
| occurrences causally related to treatment / all                     | 0 / 0   | 0 / 0   | 0 / 4   |
| deaths causally related to treatment / all                          | 0 / 0   | 0 / 0   | 0 / 0   |
| Malignant neoplasm progression                                      |   |   |   |
| subjects affected / exposed   | 0 / 9 (0.00%)   | 0 / 21 (0.00%)  | 0 / 20 (0.00%)  |
| occurrences causally related to treatment / all                     | 0 / 0   | 0 / 0   | 0 / 0   |
| deaths causally related to treatment / all                          | 0 / 0   | 0 / 0   | 0 / 0   |
| Metastases to spinal cord   |   |   |   |
| subjects affected / exposed   | 0 / 9 (0.00%)   | 0 / 21 (0.00%)  | 0 / 20 (0.00%)  |
| occurrences causally related to treatment / all                     | 0 / 0   | 0 / 0   | 0 / 0   |
| deaths causally related to treatment / all                          | 0 / 0   | 0 / 0   | 0 / 0   |
| Tumour associated fever   |   |   |   |
| subjects affected / exposed   | 0 / 9 (0.00%)   | 0 / 21 (0.00%)  | 0 / 20 (0.00%)  |
| occurrences causally related to treatment / all                     | 0 / 0   | 0 / 0   | 0 / 0   |
| deaths causally related to treatment / all                          | 0 / 0   | 0 / 0   | 0 / 0   |
| Tumour haemorrhage  |   |   |   |

|   |               |                |                |
|---|---------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 9 (0.00%) | 0 / 21 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Tumour pain                                     |               |                |                |
| subjects affected / exposed                     | 0 / 9 (0.00%) | 0 / 21 (0.00%) | 1 / 20 (5.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Vascular disorders                              |               |                |                |
| Deep vein thrombosis                            |               |                |                |
| subjects affected / exposed                     | 0 / 9 (0.00%) | 0 / 21 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Embolism  |               |                |                |
| subjects affected / exposed                     | 0 / 9 (0.00%) | 0 / 21 (0.00%) | 1 / 20 (5.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Hypotension                                     |               |                |                |
| subjects affected / exposed                     | 0 / 9 (0.00%) | 0 / 21 (0.00%) | 1 / 20 (5.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Jugular vein distension                         |               |                |                |
| subjects affected / exposed                     | 0 / 9 (0.00%) | 1 / 21 (4.76%) | 0 / 20 (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          |
| Vascular occlusion                              |               |                |                |
| subjects affected / exposed                     | 0 / 9 (0.00%) | 0 / 21 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Surgical and medical procedures                 |               |                |                |
| Euthanasia                                      |               |                |                |
| subjects affected / exposed                     | 0 / 9 (0.00%) | 0 / 21 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| General disorders and administration            |               |                |                |



|   |               |                |                |
|---|---------------|----------------|----------------|
| site conditions                                 |               |                |                |
| Asthenia  |               |                |                |
| subjects affected / exposed                     | 0 / 9 (0.00%) | 0 / 21 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Chest pain                                      |               |                |                |
| subjects affected / exposed                     | 0 / 9 (0.00%) | 1 / 21 (4.76%) | 0 / 20 (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          |
| Death   |               |                |                |
| subjects affected / exposed                     | 0 / 9 (0.00%) | 0 / 21 (0.00%) | 1 / 20 (5.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 1          |
| Disease progression                             |               |                |                |
| subjects affected / exposed                     | 0 / 9 (0.00%) | 0 / 21 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Fatigue   |               |                |                |
| subjects affected / exposed                     | 0 / 9 (0.00%) | 1 / 21 (4.76%) | 1 / 20 (5.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 1          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| General physical health deterioration           |               |                |                |
| subjects affected / exposed                     | 0 / 9 (0.00%) | 0 / 21 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Non-cardiac chest pain                          |               |                |                |
| subjects affected / exposed                     | 0 / 9 (0.00%) | 1 / 21 (4.76%) | 1 / 20 (5.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 1          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Pain  |               |                |                |
| subjects affected / exposed                     | 0 / 9 (0.00%) | 0 / 21 (0.00%) | 1 / 20 (5.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Pyrexia   |               |                |                |

|   |                |                 |                |
|---|----------------|-----------------|----------------|
| subjects affected / exposed                     | 0 / 9 (0.00%)  | 0 / 21 (0.00%)  | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0          |
| Respiratory, thoracic and mediastinal disorders |                |                 |                |
| Bronchial obstruction                           |                |                 |                |
| subjects affected / exposed                     | 0 / 9 (0.00%)  | 0 / 21 (0.00%)  | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0          |
| Dyspnoea  |                |                 |                |
| subjects affected / exposed                     | 1 / 9 (11.11%) | 2 / 21 (9.52%)  | 1 / 20 (5.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 3           | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 1          | 0 / 0           | 0 / 0          |
| Epistaxis                                       |                |                 |                |
| subjects affected / exposed                     | 0 / 9 (0.00%)  | 0 / 21 (0.00%)  | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0          |
| Increased bronchial secretion                   |                |                 |                |
| subjects affected / exposed                     | 0 / 9 (0.00%)  | 0 / 21 (0.00%)  | 1 / 20 (5.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0          |
| Laryngeal inflammation                          |                |                 |                |
| subjects affected / exposed                     | 0 / 9 (0.00%)  | 0 / 21 (0.00%)  | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0           | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0          |
| Laryngeal obstruction                           |                |                 |                |
| subjects affected / exposed                     | 0 / 9 (0.00%)  | 1 / 21 (4.76%)  | 0 / 20 (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          |
| Pleural effusion                                |                |                 |                |
| subjects affected / exposed                     | 0 / 9 (0.00%)  | 3 / 21 (14.29%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 1 / 3           | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0          |
| Pneumonitis                                     |                |                 |                |

|   |               |                |                |
|---|---------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 9 (0.00%) | 0 / 21 (0.00%) | 1 / 20 (5.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Pneumothorax                                    |               |                |                |
| subjects affected / exposed                     | 0 / 9 (0.00%) | 0 / 21 (0.00%) | 1 / 20 (5.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Pulmonary congestion                            |               |                |                |
| subjects affected / exposed                     | 0 / 9 (0.00%) | 0 / 21 (0.00%) | 1 / 20 (5.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Pulmonary fistula                               |               |                |                |
| subjects affected / exposed                     | 0 / 9 (0.00%) | 0 / 21 (0.00%) | 1 / 20 (5.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Pulmonary haemorrhage                           |               |                |                |
| subjects affected / exposed                     | 0 / 9 (0.00%) | 0 / 21 (0.00%) | 1 / 20 (5.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 1          |
| Psychiatric disorders                           |               |                |                |
| Delirium  |               |                |                |
| subjects affected / exposed                     | 0 / 9 (0.00%) | 0 / 21 (0.00%) | 1 / 20 (5.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 1          |
| Investigations                                  |               |                |                |
| Blood bilirubin increased                       |               |                |                |
| subjects affected / exposed                     | 0 / 9 (0.00%) | 0 / 21 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Blood creatine phosphokinase MB increased       |               |                |                |
| subjects affected / exposed                     | 0 / 9 (0.00%) | 0 / 21 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |

|   |               |                |                 |
|---|---------------|----------------|-----------------|
| Blood creatine phosphokinase increased          |               |                |                 |
| subjects affected / exposed                     | 0 / 9 (0.00%) | 0 / 21 (0.00%) | 0 / 20 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0           |
| Blood creatinine increased                      |               |                |                 |
| subjects affected / exposed                     | 0 / 9 (0.00%) | 0 / 21 (0.00%) | 0 / 20 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0           |
| Electrocardiogram QT prolonged                  |               |                |                 |
| subjects affected / exposed                     | 0 / 9 (0.00%) | 0 / 21 (0.00%) | 0 / 20 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0           |
| Electrocardiogram ST segment elevation          |               |                |                 |
| subjects affected / exposed                     | 0 / 9 (0.00%) | 0 / 21 (0.00%) | 0 / 20 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0           |
| Electrocardiogram T wave inversion              |               |                |                 |
| subjects affected / exposed                     | 0 / 9 (0.00%) | 0 / 21 (0.00%) | 0 / 20 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0           |
| Platelet count decreased                        |               |                |                 |
| subjects affected / exposed                     | 0 / 9 (0.00%) | 0 / 21 (0.00%) | 2 / 20 (10.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 2 / 2           |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0           |
| Troponin I increased                            |               |                |                 |
| subjects affected / exposed                     | 0 / 9 (0.00%) | 0 / 21 (0.00%) | 1 / 20 (5.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 1 / 1           |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0           |
| Troponin T increased                            |               |                |                 |
| subjects affected / exposed                     | 0 / 9 (0.00%) | 0 / 21 (0.00%) | 0 / 20 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0           |
| Injury, poisoning and procedural                |               |                |                 |

|   |               |                |                |
|---|---------------|----------------|----------------|
| complications                                   |               |                |                |
| Fracture  |               |                |                |
| subjects affected / exposed                     | 0 / 9 (0.00%) | 0 / 21 (0.00%) | 1 / 20 (5.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Subdural haematoma                              |               |                |                |
| subjects affected / exposed                     | 0 / 9 (0.00%) | 1 / 21 (4.76%) | 0 / 20 (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          |
| Tendon rupture                                  |               |                |                |
| subjects affected / exposed                     | 0 / 9 (0.00%) | 0 / 21 (0.00%) | 1 / 20 (5.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Wound   |               |                |                |
| subjects affected / exposed                     | 0 / 9 (0.00%) | 0 / 21 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Cardiac disorders                               |               |                |                |
| Acute myocardial infarction                     |               |                |                |
| subjects affected / exposed                     | 0 / 9 (0.00%) | 0 / 21 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Atrial fibrillation                             |               |                |                |
| subjects affected / exposed                     | 0 / 9 (0.00%) | 1 / 21 (4.76%) | 0 / 20 (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 arrest                                  |               |                |                |
| subjects affected / exposed                     | 0 / 9 (0.00%) | 0 / 21 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Cardiac failure congestive                      |               |                |                |
| subjects affected / exposed                     | 0 / 9 (0.00%) | 0 / 21 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |

|   |               |                |                 |
|---|---------------|----------------|-----------------|
| Cardiogenic shock                               |               |                |                 |
| subjects affected / exposed                     | 0 / 9 (0.00%) | 0 / 21 (0.00%) | 1 / 20 (5.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0           |
| Pericardial effusion                            |               |                |                 |
| subjects affected / exposed                     | 0 / 9 (0.00%) | 0 / 21 (0.00%) | 1 / 20 (5.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0           |
| Supraventricular tachycardia                    |               |                |                 |
| subjects affected / exposed                     | 0 / 9 (0.00%) | 0 / 21 (0.00%) | 1 / 20 (5.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0           |
| Nervous system disorders                        |               |                |                 |
| Cerebrovascular accident                        |               |                |                 |
| subjects affected / exposed                     | 0 / 9 (0.00%) | 0 / 21 (0.00%) | 0 / 20 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0           |
| Headache  |               |                |                 |
| subjects affected / exposed                     | 0 / 9 (0.00%) | 0 / 21 (0.00%) | 0 / 20 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0           |
| Ischaemic stroke                                |               |                |                 |
| subjects affected / exposed                     | 0 / 9 (0.00%) | 0 / 21 (0.00%) | 0 / 20 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0           |
| Neuralgia                                       |               |                |                 |
| subjects affected / exposed                     | 0 / 9 (0.00%) | 0 / 21 (0.00%) | 1 / 20 (5.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0           |
| Seizure   |               |                |                 |
| subjects affected / exposed                     | 0 / 9 (0.00%) | 1 / 21 (4.76%) | 2 / 20 (10.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 1          | 0 / 2           |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 1           |
| Somnolence                                      |               |                |                 |

|   |               |                |                 |
|---|---------------|----------------|-----------------|
| subjects affected / exposed                     | 0 / 9 (0.00%) | 0 / 21 (0.00%) | 1 / 20 (5.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0           |
| Spinal cord compression                         |               |                |                 |
| subjects affected / exposed                     | 0 / 9 (0.00%) | 1 / 21 (4.76%) | 0 / 20 (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           |
| Syncope   |               |                |                 |
| subjects affected / exposed                     | 0 / 9 (0.00%) | 0 / 21 (0.00%) | 0 / 20 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0           |
| Blood and lymphatic system disorders            |               |                |                 |
| Anaemia   |               |                |                 |
| subjects affected / exposed                     | 0 / 9 (0.00%) | 1 / 21 (4.76%) | 0 / 20 (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           |
| Febrile neutropenia                             |               |                |                 |
| subjects affected / exposed                     | 0 / 9 (0.00%) | 0 / 21 (0.00%) | 0 / 20 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0           |
| Thrombocytopenia                                |               |                |                 |
| subjects affected / exposed                     | 0 / 9 (0.00%) | 1 / 21 (4.76%) | 2 / 20 (10.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 1 / 1          | 2 / 2           |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0           |
| Eye disorders                                   |               |                |                 |
| Eye haemorrhage                                 |               |                |                 |
| subjects affected / exposed                     | 0 / 9 (0.00%) | 1 / 21 (4.76%) | 0 / 20 (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           |
| Uveitis   |               |                |                 |
| subjects affected / exposed                     | 0 / 9 (0.00%) | 0 / 21 (0.00%) | 0 / 20 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0           |
| Gastrointestinal disorders                      |               |                |                 |

|   |               |                |                |
|---|---------------|----------------|----------------|
| Abdominal pain                                  |               |                |                |
| subjects affected / exposed                     | 0 / 9 (0.00%) | 0 / 21 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Abdominal pain upper                            |               |                |                |
| subjects affected / exposed                     | 0 / 9 (0.00%) | 0 / 21 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Diarrhoea                                       |               |                |                |
| subjects affected / exposed                     | 0 / 9 (0.00%) | 0 / 21 (0.00%) | 1 / 20 (5.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Duodenal ulcer                                  |               |                |                |
| subjects affected / exposed                     | 0 / 9 (0.00%) | 0 / 21 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Gastrointestinal haemorrhage                    |               |                |                |
| subjects affected / exposed                     | 0 / 9 (0.00%) | 0 / 21 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Lower gastrointestinal haemorrhage              |               |                |                |
| subjects affected / exposed                     | 0 / 9 (0.00%) | 0 / 21 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Nausea  |               |                |                |
| subjects affected / exposed                     | 0 / 9 (0.00%) | 0 / 21 (0.00%) | 1 / 20 (5.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Oral pain                                       |               |                |                |
| subjects affected / exposed                     | 0 / 9 (0.00%) | 0 / 21 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Small intestinal haemorrhage                    |               |                |                |



|   |               |                |                 |
|---|---------------|----------------|-----------------|
| subjects affected / exposed                     | 0 / 9 (0.00%) | 0 / 21 (0.00%) | 0 / 20 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0           |
| Small intestinal obstruction                    |               |                |                 |
| subjects affected / exposed                     | 0 / 9 (0.00%) | 0 / 21 (0.00%) | 0 / 20 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0           |
| Upper gastrointestinal haemorrhage              |               |                |                 |
| subjects affected / exposed                     | 0 / 9 (0.00%) | 0 / 21 (0.00%) | 0 / 20 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0           |
| Vomiting  |               |                |                 |
| subjects affected / exposed                     | 0 / 9 (0.00%) | 0 / 21 (0.00%) | 2 / 20 (10.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 2           |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0           |
| Hepatobiliary disorders                         |               |                |                 |
| Biliary obstruction                             |               |                |                 |
| subjects affected / exposed                     | 0 / 9 (0.00%) | 0 / 21 (0.00%) | 0 / 20 (0.00%)  |
| 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 / 9 (0.00%) | 0 / 21 (0.00%) | 0 / 20 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0           |
| Skin and subcutaneous tissue disorders          |               |                |                 |
| Dermatitis acneiform                            |               |                |                 |
| subjects affected / exposed                     | 0 / 9 (0.00%) | 0 / 21 (0.00%) | 0 / 20 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0           |
| Pruritus  |               |                |                 |
| subjects affected / exposed                     | 0 / 9 (0.00%) | 0 / 21 (0.00%) | 1 / 20 (5.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0           |
| Skin necrosis                                   |               |                |                 |

|   |               |                |                |
|---|---------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 9 (0.00%) | 0 / 21 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Renal and urinary disorders                     |               |                |                |
| Acute kidney injury                             |               |                |                |
| subjects affected / exposed                     | 0 / 9 (0.00%) | 1 / 21 (4.76%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 1          | 0 / 0          |
| Bladder dilatation                              |               |                |                |
| subjects affected / exposed                     | 0 / 9 (0.00%) | 0 / 21 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Calculus urinary                                |               |                |                |
| subjects affected / exposed                     | 0 / 9 (0.00%) | 1 / 21 (4.76%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Haematuria                                      |               |                |                |
| subjects affected / exposed                     | 0 / 9 (0.00%) | 0 / 21 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Urinary retention                               |               |                |                |
| subjects affected / exposed                     | 0 / 9 (0.00%) | 0 / 21 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Musculoskeletal and connective tissue disorders |               |                |                |
| Arthralgia                                      |               |                |                |
| subjects affected / exposed                     | 0 / 9 (0.00%) | 0 / 21 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Osteonecrosis of jaw                            |               |                |                |
| subjects affected / exposed                     | 0 / 9 (0.00%) | 0 / 21 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |

|   |               |                |                |
|---|---------------|----------------|----------------|
| Pain in extremity                               |               |                |                |
| subjects affected / exposed                     | 0 / 9 (0.00%) | 0 / 21 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Pain in jaw                                     |               |                |                |
| subjects affected / exposed                     | 0 / 9 (0.00%) | 1 / 21 (4.76%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Infections and infestations                     |               |                |                |
| Abdominal infection                             |               |                |                |
| subjects affected / exposed                     | 0 / 9 (0.00%) | 0 / 21 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Bronchitis                                      |               |                |                |
| subjects affected / exposed                     | 0 / 9 (0.00%) | 0 / 21 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| COVID-19  |               |                |                |
| subjects affected / exposed                     | 0 / 9 (0.00%) | 1 / 21 (4.76%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 1          | 0 / 0          |
| Cystitis  |               |                |                |
| subjects affected / exposed                     | 0 / 9 (0.00%) | 0 / 21 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Dacryocystitis                                  |               |                |                |
| subjects affected / exposed                     | 0 / 9 (0.00%) | 1 / 21 (4.76%) | 0 / 20 (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          |
| Device related infection                        |               |                |                |
| subjects affected / exposed                     | 0 / 9 (0.00%) | 0 / 21 (0.00%) | 0 / 20 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Hepatic infection                               |               |                |                |

|   |                |                |                 |
|---|----------------|----------------|-----------------|
| subjects affected / exposed                     | 0 / 9 (0.00%)  | 0 / 21 (0.00%) | 0 / 20 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Infection                                       |                |                |                 |
| subjects affected / exposed                     | 0 / 9 (0.00%)  | 0 / 21 (0.00%) | 0 / 20 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Influenza                                       |                |                |                 |
| subjects affected / exposed                     | 0 / 9 (0.00%)  | 0 / 21 (0.00%) | 0 / 20 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Localised infection                             |                |                |                 |
| subjects affected / exposed                     | 0 / 9 (0.00%)  | 0 / 21 (0.00%) | 0 / 20 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Lower respiratory tract infection               |                |                |                 |
| subjects affected / exposed                     | 0 / 9 (0.00%)  | 0 / 21 (0.00%) | 1 / 20 (5.00%)  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Meningitis pneumococcal                         |                |                |                 |
| subjects affected / exposed                     | 0 / 9 (0.00%)  | 0 / 21 (0.00%) | 0 / 20 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Periorbital cellulitis                          |                |                |                 |
| subjects affected / exposed                     | 0 / 9 (0.00%)  | 1 / 21 (4.76%) | 0 / 20 (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                                       |                |                |                 |
| subjects affected / exposed                     | 1 / 9 (11.11%) | 1 / 21 (4.76%) | 5 / 20 (25.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 1          | 0 / 5           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 1          | 0 / 0           |
| Pneumonia aspiration                            |                |                |                 |

|   |               |                |                 |
|---|---------------|----------------|-----------------|
| subjects affected / exposed                     | 0 / 9 (0.00%) | 0 / 21 (0.00%) | 1 / 20 (5.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0           |
| Sepsis  |               |                |                 |
| subjects affected / exposed                     | 0 / 9 (0.00%) | 0 / 21 (0.00%) | 1 / 20 (5.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 1           |
| Spinal cord infection                           |               |                |                 |
| subjects affected / exposed                     | 0 / 9 (0.00%) | 0 / 21 (0.00%) | 0 / 20 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0           |
| Urinary tract infection                         |               |                |                 |
| subjects affected / exposed                     | 0 / 9 (0.00%) | 0 / 21 (0.00%) | 0 / 20 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0           |
| Metabolism and nutrition disorders              |               |                |                 |
| Dehydration                                     |               |                |                 |
| subjects affected / exposed                     | 0 / 9 (0.00%) | 0 / 21 (0.00%) | 0 / 20 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0           |
| Hypercalcaemia                                  |               |                |                 |
| subjects affected / exposed                     | 0 / 9 (0.00%) | 0 / 21 (0.00%) | 3 / 20 (15.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 5           |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0           |
| Hyperglycaemia                                  |               |                |                 |
| subjects affected / exposed                     | 0 / 9 (0.00%) | 0 / 21 (0.00%) | 0 / 20 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0           |
| Hypokalaemia                                    |               |                |                 |
| subjects affected / exposed                     | 0 / 9 (0.00%) | 0 / 21 (0.00%) | 0 / 20 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0           |
| Hyponatraemia                                   |               |                |                 |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 1 / 9 (11.11%) | 0 / 21 (0.00%) | 0 / 20 (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          |
| Hypophosphataemia                               |                |                |                |
| subjects affected / exposed                     | 0 / 9 (0.00%)  | 0 / 21 (0.00%) | 1 / 20 (5.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |

| <b>Serious adverse events</b>                                       | Phase Ib - Schedule B: 2 mg BI 894999 (mCRPC patients) | Phase Ib - Schedule B: 2.5 mg BI 894999 (mCRPC patients) | Phase Ib - Schedule B: 2.5 mg BI 894999 (CRC patients) |
|---|--|--|--|
| Total subjects affected by serious adverse events                   |  |  |  |
| subjects affected / exposed   | 1 / 1 (100.00%)  | 8 / 10 (80.00%)  | 8 / 14 (57.14%)  |
| number of deaths (all causes)                                       | 0  | 0  | 0  |
| number of deaths resulting from adverse events                      | 0  | 0  | 0  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |  |  |  |
| Cancer pain   |  |  |  |
| subjects affected / exposed   | 0 / 1 (0.00%)  | 0 / 10 (0.00%)   | 0 / 14 (0.00%)   |
| occurrences causally related to treatment / all                     | 0 / 0  | 0 / 0  | 0 / 0  |
| deaths causally related to treatment / all                          | 0 / 0  | 0 / 0  | 0 / 0  |
| Malignant neoplasm progression                                      |  |  |  |
| subjects affected / exposed   | 0 / 1 (0.00%)  | 0 / 10 (0.00%)   | 0 / 14 (0.00%)   |
| occurrences causally related to treatment / all                     | 0 / 0  | 0 / 0  | 0 / 0  |
| deaths causally related to treatment / all                          | 0 / 0  | 0 / 0  | 0 / 0  |
| Metastases to spinal cord   |  |  |  |
| subjects affected / exposed   | 0 / 1 (0.00%)  | 0 / 10 (0.00%)   | 0 / 14 (0.00%)   |
| occurrences causally related to treatment / all                     | 0 / 0  | 0 / 0  | 0 / 0  |
| deaths causally related to treatment / all                          | 0 / 0  | 0 / 0  | 0 / 0  |
| Tumour associated fever   |  |  |  |
| subjects affected / exposed   | 0 / 1 (0.00%)  | 0 / 10 (0.00%)   | 0 / 14 (0.00%)   |
| occurrences causally related to treatment / all                     | 0 / 0  | 0 / 0  | 0 / 0  |
| deaths causally related to treatment / all                          | 0 / 0  | 0 / 0  | 0 / 0  |
| Tumour haemorrhage  |  |  |  |

|   |               |                 |                |
|---|---------------|-----------------|----------------|
| subjects affected / exposed                     | 0 / 1 (0.00%) | 1 / 10 (10.00%) | 0 / 14 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 1           | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0           | 0 / 0          |
| Tumour pain                                     |               |                 |                |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 1 / 10 (10.00%) | 0 / 14 (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          |
| Vascular disorders                              |               |                 |                |
| Deep vein thrombosis                            |               |                 |                |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 1 / 10 (10.00%) | 0 / 14 (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          |
| Embolism  |               |                 |                |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 10 (0.00%)  | 0 / 14 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0           | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0           | 0 / 0          |
| Hypotension                                     |               |                 |                |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 10 (0.00%)  | 0 / 14 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0           | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0           | 0 / 0          |
| Jugular vein distension                         |               |                 |                |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 10 (0.00%)  | 0 / 14 (0.00%) |
| 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 occlusion                              |               |                 |                |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 1 / 10 (10.00%) | 0 / 14 (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          |
| Surgical and medical procedures                 |               |                 |                |
| Euthanasia                                      |               |                 |                |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 10 (0.00%)  | 0 / 14 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0           | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0           | 0 / 0          |
| General disorders and administration            |               |                 |                |

|   |               |                |                |
|---|---------------|----------------|----------------|
| site conditions                                 |               |                |                |
| Asthenia  |               |                |                |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 10 (0.00%) | 0 / 14 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Chest pain                                      |               |                |                |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 10 (0.00%) | 0 / 14 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Death   |               |                |                |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 10 (0.00%) | 0 / 14 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Disease progression                             |               |                |                |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 10 (0.00%) | 0 / 14 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Fatigue   |               |                |                |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 10 (0.00%) | 0 / 14 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| General physical health deterioration           |               |                |                |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 10 (0.00%) | 0 / 14 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Non-cardiac chest pain                          |               |                |                |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 10 (0.00%) | 0 / 14 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Pain  |               |                |                |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 10 (0.00%) | 0 / 14 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Pyrexia   |               |                |                |



|   |               |                 |                |
|---|---------------|-----------------|----------------|
| subjects affected / exposed                     | 0 / 1 (0.00%) | 1 / 10 (10.00%) | 0 / 14 (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 |               |                 |                |
| Bronchial obstruction                           |               |                 |                |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 1 / 10 (10.00%) | 0 / 14 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 1           | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0           | 0 / 0          |
| Dyspnoea  |               |                 |                |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 1 / 10 (10.00%) | 0 / 14 (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          |
| Epistaxis                                       |               |                 |                |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 10 (0.00%)  | 0 / 14 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0           | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0           | 0 / 0          |
| Increased bronchial secretion                   |               |                 |                |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 10 (0.00%)  | 0 / 14 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0           | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0           | 0 / 0          |
| Laryngeal inflammation                          |               |                 |                |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 10 (0.00%)  | 0 / 14 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0           | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0           | 0 / 0          |
| Laryngeal obstruction                           |               |                 |                |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 10 (0.00%)  | 0 / 14 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0           | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0           | 0 / 0          |
| Pleural effusion                                |               |                 |                |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 10 (0.00%)  | 1 / 14 (7.14%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0           | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0           | 0 / 0          |
| Pneumonitis                                     |               |                 |                |

|   |               |                |                |
|---|---------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 10 (0.00%) | 0 / 14 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Pneumothorax                                    |               |                |                |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 10 (0.00%) | 0 / 14 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Pulmonary congestion                            |               |                |                |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 10 (0.00%) | 0 / 14 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Pulmonary fistula                               |               |                |                |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 10 (0.00%) | 0 / 14 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Pulmonary haemorrhage                           |               |                |                |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 10 (0.00%) | 0 / 14 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Psychiatric disorders                           |               |                |                |
| Delirium  |               |                |                |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 10 (0.00%) | 0 / 14 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Investigations                                  |               |                |                |
| Blood bilirubin increased                       |               |                |                |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 10 (0.00%) | 0 / 14 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Blood creatine phosphokinase MB increased       |               |                |                |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 10 (0.00%) | 0 / 14 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |

|   |                 |                |                |  |
|---|-----------------|----------------|----------------|--|
| Blood creatine phosphokinase increased          |                 |                |                |  |
| subjects affected / exposed                     | 0 / 1 (0.00%)   | 0 / 10 (0.00%) | 0 / 14 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0          |  |
| Blood creatinine increased                      |                 |                |                |  |
| subjects affected / exposed                     | 0 / 1 (0.00%)   | 0 / 10 (0.00%) | 0 / 14 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0          |  |
| Electrocardiogram QT prolonged                  |                 |                |                |  |
| subjects affected / exposed                     | 0 / 1 (0.00%)   | 0 / 10 (0.00%) | 0 / 14 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0          |  |
| Electrocardiogram ST segment elevation          |                 |                |                |  |
| subjects affected / exposed                     | 0 / 1 (0.00%)   | 0 / 10 (0.00%) | 0 / 14 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0          |  |
| Electrocardiogram T wave inversion              |                 |                |                |  |
| subjects affected / exposed                     | 0 / 1 (0.00%)   | 0 / 10 (0.00%) | 0 / 14 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0          |  |
| Platelet count decreased                        |                 |                |                |  |
| subjects affected / exposed                     | 1 / 1 (100.00%) | 0 / 10 (0.00%) | 0 / 14 (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          |  |
| Troponin I increased                            |                 |                |                |  |
| subjects affected / exposed                     | 0 / 1 (0.00%)   | 0 / 10 (0.00%) | 0 / 14 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0          |  |
| Troponin T increased                            |                 |                |                |  |
| subjects affected / exposed                     | 0 / 1 (0.00%)   | 0 / 10 (0.00%) | 0 / 14 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0          |  |
| Injury, poisoning and procedural                |                 |                |                |  |

|   |               |                |                |
|---|---------------|----------------|----------------|
| complications                                   |               |                |                |
| Fracture  |               |                |                |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 10 (0.00%) | 0 / 14 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Subdural haematoma                              |               |                |                |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 10 (0.00%) | 0 / 14 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Tendon rupture                                  |               |                |                |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 10 (0.00%) | 0 / 14 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Wound   |               |                |                |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 10 (0.00%) | 0 / 14 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Cardiac disorders                               |               |                |                |
| Acute myocardial infarction                     |               |                |                |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 10 (0.00%) | 0 / 14 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Atrial fibrillation                             |               |                |                |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 10 (0.00%) | 0 / 14 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Cardiac arrest                                  |               |                |                |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 10 (0.00%) | 0 / 14 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Cardiac failure congestive                      |               |                |                |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 10 (0.00%) | 1 / 14 (7.14%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |

|   |               |                |                |
|---|---------------|----------------|----------------|
| Cardiogenic shock                               |               |                |                |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 10 (0.00%) | 0 / 14 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Pericardial effusion                            |               |                |                |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 10 (0.00%) | 0 / 14 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Supraventricular tachycardia                    |               |                |                |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 10 (0.00%) | 0 / 14 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Nervous system disorders                        |               |                |                |
| Cerebrovascular accident                        |               |                |                |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 10 (0.00%) | 0 / 14 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Headache  |               |                |                |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 10 (0.00%) | 0 / 14 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Ischaemic stroke                                |               |                |                |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 10 (0.00%) | 1 / 14 (7.14%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Neuralgia                                       |               |                |                |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 10 (0.00%) | 0 / 14 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Seizure   |               |                |                |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 10 (0.00%) | 1 / 14 (7.14%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Somnolence                                      |               |                |                |

|   |               |                |                |
|---|---------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 10 (0.00%) | 0 / 14 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Spinal cord compression                         |               |                |                |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 10 (0.00%) | 0 / 14 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Syncope   |               |                |                |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 10 (0.00%) | 0 / 14 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Blood and lymphatic system disorders            |               |                |                |
| Anaemia   |               |                |                |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 10 (0.00%) | 0 / 14 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Febrile neutropenia                             |               |                |                |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 10 (0.00%) | 0 / 14 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Thrombocytopenia                                |               |                |                |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 10 (0.00%) | 0 / 14 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Eye disorders                                   |               |                |                |
| Eye haemorrhage                                 |               |                |                |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 10 (0.00%) | 0 / 14 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Uveitis   |               |                |                |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 10 (0.00%) | 0 / 14 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Gastrointestinal disorders                      |               |                |                |

|   |               |                 |                |
|---|---------------|-----------------|----------------|
| Abdominal pain                                  |               |                 |                |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 10 (0.00%)  | 1 / 14 (7.14%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0           | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0           | 0 / 0          |
| Abdominal pain upper                            |               |                 |                |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 10 (0.00%)  | 0 / 14 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0           | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0           | 0 / 0          |
| Diarrhoea                                       |               |                 |                |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 10 (0.00%)  | 1 / 14 (7.14%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0           | 1 / 1          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0           | 0 / 0          |
| Duodenal ulcer                                  |               |                 |                |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 10 (0.00%)  | 0 / 14 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0           | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0           | 0 / 0          |
| Gastrointestinal haemorrhage                    |               |                 |                |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 10 (0.00%)  | 0 / 14 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0           | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0           | 0 / 0          |
| Lower gastrointestinal haemorrhage              |               |                 |                |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 1 / 10 (10.00%) | 0 / 14 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 1           | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0           | 0 / 0          |
| Nausea  |               |                 |                |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 1 / 10 (10.00%) | 0 / 14 (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          |
| Oral pain                                       |               |                 |                |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 10 (0.00%)  | 0 / 14 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0           | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0           | 0 / 0          |
| Small intestinal haemorrhage                    |               |                 |                |

|   |               |                |                 |
|---|---------------|----------------|-----------------|
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 10 (0.00%) | 0 / 14 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0           |
| Small intestinal obstruction                    |               |                |                 |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 10 (0.00%) | 1 / 14 (7.14%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0           |
| Upper gastrointestinal haemorrhage              |               |                |                 |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 10 (0.00%) | 0 / 14 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0           |
| Vomiting  |               |                |                 |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 10 (0.00%) | 3 / 14 (21.43%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 2 / 3           |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0           |
| Hepatobiliary disorders                         |               |                |                 |
| Biliary obstruction                             |               |                |                 |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 10 (0.00%) | 0 / 14 (0.00%)  |
| 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 / 1 (0.00%) | 0 / 10 (0.00%) | 0 / 14 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0           |
| Skin and subcutaneous tissue disorders          |               |                |                 |
| Dermatitis acneiform                            |               |                |                 |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 10 (0.00%) | 1 / 14 (7.14%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 1 / 1           |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0           |
| Pruritus  |               |                |                 |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 10 (0.00%) | 0 / 14 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0           |
| Skin necrosis                                   |               |                |                 |



|   |               |                 |                |
|---|---------------|-----------------|----------------|
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 10 (0.00%)  | 0 / 14 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0           | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0           | 0 / 0          |
| Renal and urinary disorders                     |               |                 |                |
| Acute kidney injury                             |               |                 |                |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 1 / 10 (10.00%) | 0 / 14 (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          |
| Bladder dilatation                              |               |                 |                |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 1 / 10 (10.00%) | 0 / 14 (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          |
| Calculus urinary                                |               |                 |                |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 10 (0.00%)  | 0 / 14 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0           | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0           | 0 / 0          |
| Haematuria                                      |               |                 |                |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 10 (0.00%)  | 0 / 14 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0           | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0           | 0 / 0          |
| Urinary retention                               |               |                 |                |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 1 / 10 (10.00%) | 0 / 14 (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          |
| Musculoskeletal and connective tissue disorders |               |                 |                |
| Arthralgia                                      |               |                 |                |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 10 (0.00%)  | 0 / 14 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0           | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0           | 0 / 0          |
| Osteonecrosis of jaw                            |               |                 |                |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 10 (0.00%)  | 0 / 14 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0           | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0           | 0 / 0          |

|   |               |                |                |
|---|---------------|----------------|----------------|
| Pain in extremity                               |               |                |                |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 10 (0.00%) | 0 / 14 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Pain in jaw                                     |               |                |                |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 10 (0.00%) | 0 / 14 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Infections and infestations                     |               |                |                |
| Abdominal infection                             |               |                |                |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 10 (0.00%) | 0 / 14 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Bronchitis                                      |               |                |                |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 10 (0.00%) | 0 / 14 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| COVID-19  |               |                |                |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 10 (0.00%) | 0 / 14 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Cystitis  |               |                |                |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 10 (0.00%) | 0 / 14 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Dacryocystitis                                  |               |                |                |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 10 (0.00%) | 0 / 14 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Device related infection                        |               |                |                |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 10 (0.00%) | 0 / 14 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Hepatic infection                               |               |                |                |

|   |               |                |                |
|---|---------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 10 (0.00%) | 1 / 14 (7.14%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Infection                                       |               |                |                |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 10 (0.00%) | 0 / 14 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Influenza                                       |               |                |                |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 10 (0.00%) | 0 / 14 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Localised infection                             |               |                |                |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 10 (0.00%) | 0 / 14 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Lower respiratory tract infection               |               |                |                |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 10 (0.00%) | 0 / 14 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Meningitis pneumococcal                         |               |                |                |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 10 (0.00%) | 0 / 14 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Periorbital cellulitis                          |               |                |                |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 10 (0.00%) | 0 / 14 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Pneumonia                                       |               |                |                |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 10 (0.00%) | 0 / 14 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Pneumonia aspiration                            |               |                |                |

|   |               |                 |                |
|---|---------------|-----------------|----------------|
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 10 (0.00%)  | 0 / 14 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0           | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0           | 0 / 0          |
| Sepsis  |               |                 |                |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 10 (0.00%)  | 0 / 14 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0           | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0           | 0 / 0          |
| Spinal cord infection                           |               |                 |                |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 1 / 10 (10.00%) | 0 / 14 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 1           | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0           | 0 / 0          |
| Urinary tract infection                         |               |                 |                |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 1 / 10 (10.00%) | 1 / 14 (7.14%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 1           | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0           | 0 / 0          |
| Metabolism and nutrition disorders              |               |                 |                |
| Dehydration                                     |               |                 |                |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 10 (0.00%)  | 1 / 14 (7.14%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0           | 1 / 1          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0           | 0 / 0          |
| Hypercalcaemia                                  |               |                 |                |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 10 (0.00%)  | 0 / 14 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0           | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0           | 0 / 0          |
| Hyperglycaemia                                  |               |                 |                |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 10 (0.00%)  | 1 / 14 (7.14%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0           | 1 / 1          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0           | 0 / 0          |
| Hypokalaemia                                    |               |                 |                |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 0 / 10 (0.00%)  | 0 / 14 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0           | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0           | 0 / 0          |
| Hyponatraemia                                   |               |                 |                |

|   |               |                 |                |
|---|---------------|-----------------|----------------|
| subjects affected / exposed                     | 0 / 1 (0.00%) | 1 / 10 (10.00%) | 0 / 14 (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          |
| Hypophosphataemia                               |               |                 |                |
| subjects affected / exposed                     | 0 / 1 (0.00%) | 1 / 10 (10.00%) | 0 / 14 (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>                                       | Phase Ib - Schedule C: BI 894999 7/3.5 mg (NC patients) |  |  |
| Total subjects affected by serious adverse events                   |   |  |  |
| subjects affected / exposed   | 1 / 1 (100.00%)   |  |  |
| number of deaths (all causes)                                       | 0   |  |  |
| number of deaths resulting from adverse events                      | 0   |  |  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |   |  |  |
| Cancer pain   |   |  |  |
| subjects affected / exposed   | 0 / 1 (0.00%)   |  |  |
| occurrences causally related to treatment / all                     | 0 / 0   |  |  |
| deaths causally related to treatment / all                          | 0 / 0   |  |  |
| Malignant neoplasm progression                                      |   |  |  |
| subjects affected / exposed   | 0 / 1 (0.00%)   |  |  |
| occurrences causally related to treatment / all                     | 0 / 0   |  |  |
| deaths causally related to treatment / all                          | 0 / 0   |  |  |
| Metastases to spinal cord   |   |  |  |
| subjects affected / exposed   | 0 / 1 (0.00%)   |  |  |
| occurrences causally related to treatment / all                     | 0 / 0   |  |  |
| deaths causally related to treatment / all                          | 0 / 0   |  |  |
| Tumour associated fever   |   |  |  |
| subjects affected / exposed   | 0 / 1 (0.00%)   |  |  |
| occurrences causally related to treatment / all                     | 0 / 0   |  |  |
| deaths causally related to treatment / all                          | 0 / 0   |  |  |
| Tumour haemorrhage  |   |  |  |

|   |               |  |  |
|---|---------------|--|--|
| subjects affected / exposed                     | 0 / 1 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Tumour pain                                     |               |  |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Vascular disorders                              |               |  |  |
| Deep vein thrombosis                            |               |  |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Embolism  |               |  |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Hypotension                                     |               |  |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Jugular vein distension                         |               |  |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Vascular occlusion                              |               |  |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Surgical and medical procedures                 |               |  |  |
| Euthanasia                                      |               |  |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| General disorders and administration            |               |  |  |

|   |                 |  |  |  |
|---|-----------------|--|--|--|
| site conditions                                 |                 |  |  |  |
| Asthenia  |                 |  |  |  |
| subjects affected / exposed                     | 0 / 1 (0.00%)   |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| Chest pain                                      |                 |  |  |  |
| subjects affected / exposed                     | 0 / 1 (0.00%)   |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| Death   |                 |  |  |  |
| subjects affected / exposed                     | 0 / 1 (0.00%)   |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| Disease progression                             |                 |  |  |  |
| subjects affected / exposed                     | 0 / 1 (0.00%)   |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| Fatigue   |                 |  |  |  |
| subjects affected / exposed                     | 1 / 1 (100.00%) |  |  |  |
| occurrences causally related to treatment / all | 1 / 1           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| General physical health deterioration           |                 |  |  |  |
| subjects affected / exposed                     | 0 / 1 (0.00%)   |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| Non-cardiac chest pain                          |                 |  |  |  |
| subjects affected / exposed                     | 0 / 1 (0.00%)   |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| Pain  |                 |  |  |  |
| subjects affected / exposed                     | 0 / 1 (0.00%)   |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| Pyrexia   |                 |  |  |  |

|   |               |  |  |
|---|---------------|--|--|
| subjects affected / exposed                     | 0 / 1 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Respiratory, thoracic and mediastinal disorders |               |  |  |
| Bronchial obstruction                           |               |  |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Dyspnoea  |               |  |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Epistaxis                                       |               |  |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Increased bronchial secretion                   |               |  |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Laryngeal inflammation                          |               |  |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Laryngeal obstruction                           |               |  |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Pleural effusion                                |               |  |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Pneumonitis                                     |               |  |  |



|   |                 |  |  |
|---|-----------------|--|--|
| subjects affected / exposed                     | 0 / 1 (0.00%)   |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Pneumothorax                                    |                 |  |  |
| subjects affected / exposed                     | 0 / 1 (0.00%)   |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Pulmonary congestion                            |                 |  |  |
| subjects affected / exposed                     | 0 / 1 (0.00%)   |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Pulmonary fistula                               |                 |  |  |
| subjects affected / exposed                     | 0 / 1 (0.00%)   |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Pulmonary haemorrhage                           |                 |  |  |
| subjects affected / exposed                     | 1 / 1 (100.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Psychiatric disorders                           |                 |  |  |
| Delirium  |                 |  |  |
| subjects affected / exposed                     | 0 / 1 (0.00%)   |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Investigations                                  |                 |  |  |
| Blood bilirubin increased                       |                 |  |  |
| subjects affected / exposed                     | 0 / 1 (0.00%)   |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Blood creatine phosphokinase MB increased       |                 |  |  |
| subjects affected / exposed                     | 0 / 1 (0.00%)   |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |

|   |                 |  |  |  |
|---|-----------------|--|--|--|
| Blood creatine phosphokinase increased          |                 |  |  |  |
| subjects affected / exposed                     | 0 / 1 (0.00%)   |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| Blood creatinine increased                      |                 |  |  |  |
| subjects affected / exposed                     | 0 / 1 (0.00%)   |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| Electrocardiogram QT prolonged                  |                 |  |  |  |
| subjects affected / exposed                     | 0 / 1 (0.00%)   |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| Electrocardiogram ST segment elevation          |                 |  |  |  |
| subjects affected / exposed                     | 0 / 1 (0.00%)   |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| Electrocardiogram T wave inversion              |                 |  |  |  |
| subjects affected / exposed                     | 0 / 1 (0.00%)   |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| Platelet count decreased                        |                 |  |  |  |
| subjects affected / exposed                     | 1 / 1 (100.00%) |  |  |  |
| occurrences causally related to treatment / all | 2 / 2           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| Troponin I increased                            |                 |  |  |  |
| subjects affected / exposed                     | 0 / 1 (0.00%)   |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| Troponin T increased                            |                 |  |  |  |
| subjects affected / exposed                     | 0 / 1 (0.00%)   |  |  |  |
| occurrences causally related to treatment / all | 0 / 0           |  |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |  |
| Injury, poisoning and procedural                |                 |  |  |  |

|   |               |  |  |  |
|---|---------------|--|--|--|
| complications                                   |               |  |  |  |
| Fracture  |               |  |  |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |  |
| Subdural haematoma                              |               |  |  |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |  |
| Tendon rupture                                  |               |  |  |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |  |
| Wound   |               |  |  |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |  |
| Cardiac disorders                               |               |  |  |  |
| Acute myocardial infarction                     |               |  |  |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |  |
| Atrial fibrillation                             |               |  |  |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |  |
| Cardiac arrest                                  |               |  |  |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |  |
| Cardiac failure congestive                      |               |  |  |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |  |

|   |               |  |  |  |
|---|---------------|--|--|--|
| Cardiogenic shock                               |               |  |  |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |  |
| Pericardial effusion                            |               |  |  |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |  |
| Supraventricular tachycardia                    |               |  |  |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |  |
| Nervous system disorders                        |               |  |  |  |
| Cerebrovascular accident                        |               |  |  |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |  |
| Headache  |               |  |  |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |  |
| Ischaemic stroke                                |               |  |  |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |  |
| Neuralgia                                       |               |  |  |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |  |
| Seizure   |               |  |  |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |  |
| Somnolence                                      |               |  |  |  |

|   |               |  |  |
|---|---------------|--|--|
| subjects affected / exposed                     | 0 / 1 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Spinal cord compression                         |               |  |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Syncope   |               |  |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Blood and lymphatic system disorders            |               |  |  |
| Anaemia   |               |  |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Febrile neutropenia                             |               |  |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Thrombocytopenia                                |               |  |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Eye disorders                                   |               |  |  |
| Eye haemorrhage                                 |               |  |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Uveitis   |               |  |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Gastrointestinal disorders                      |               |  |  |

|   |               |  |  |  |
|---|---------------|--|--|--|
| Abdominal pain                                  |               |  |  |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |  |
| Abdominal pain upper                            |               |  |  |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |  |
| Diarrhoea                                       |               |  |  |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |  |
| Duodenal ulcer                                  |               |  |  |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |  |
| Gastrointestinal haemorrhage                    |               |  |  |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |  |
| Lower gastrointestinal haemorrhage              |               |  |  |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |  |
| Nausea  |               |  |  |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |  |
| Oral pain                                       |               |  |  |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |  |
| Small intestinal haemorrhage                    |               |  |  |  |

|   |               |  |  |
|---|---------------|--|--|
| subjects affected / exposed                     | 0 / 1 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Small intestinal obstruction                    |               |  |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Upper gastrointestinal haemorrhage              |               |  |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Vomiting  |               |  |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Hepatobiliary disorders                         |               |  |  |
| Biliary obstruction                             |               |  |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Cholangitis                                     |               |  |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Skin and subcutaneous tissue disorders          |               |  |  |
| Dermatitis acneiform                            |               |  |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Pruritus  |               |  |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Skin necrosis                                   |               |  |  |

|   |               |  |  |
|---|---------------|--|--|
| subjects affected / exposed                     | 0 / 1 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Renal and urinary disorders                     |               |  |  |
| Acute kidney injury                             |               |  |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Bladder dilatation                              |               |  |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Calculus urinary                                |               |  |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Haematuria                                      |               |  |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Urinary retention                               |               |  |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Musculoskeletal and connective tissue disorders |               |  |  |
| Arthralgia                                      |               |  |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Osteonecrosis of jaw                            |               |  |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |



|   |               |  |  |
|---|---------------|--|--|
| Pain in extremity                               |               |  |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Pain in jaw                                     |               |  |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Infections and infestations                     |               |  |  |
| Abdominal infection                             |               |  |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Bronchitis                                      |               |  |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| COVID-19  |               |  |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Cystitis  |               |  |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Dacryocystitis                                  |               |  |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Device related infection                        |               |  |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Hepatic infection                               |               |  |  |

|   |               |  |  |  |
|---|---------------|--|--|--|
| subjects affected / exposed                     | 0 / 1 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |  |
| Infection                                       |               |  |  |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |  |
| Influenza                                       |               |  |  |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |  |
| Localised infection                             |               |  |  |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |  |
| Lower respiratory tract infection               |               |  |  |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |  |
| Meningitis pneumococcal                         |               |  |  |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |  |
| Periorbital cellulitis                          |               |  |  |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |  |
| Pneumonia                                       |               |  |  |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) |  |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |  |
| Pneumonia aspiration                            |               |  |  |  |

|   |               |  |  |
|---|---------------|--|--|
| subjects affected / exposed                     | 0 / 1 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Sepsis  |               |  |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Spinal cord infection                           |               |  |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Urinary tract infection                         |               |  |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Metabolism and nutrition disorders              |               |  |  |
| Dehydration                                     |               |  |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Hypercalcaemia                                  |               |  |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Hyperglycaemia                                  |               |  |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Hypokalaemia                                    |               |  |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Hyponatraemia                                   |               |  |  |

|   |               |  |  |
|---|---------------|--|--|
| subjects affected / exposed                     | 0 / 1 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |
| Hypophosphataemia                               |               |  |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0         |  |  |
| deaths causally related to treatment / all      | 0 / 0         |  |  |

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

| <b>Non-serious adverse events</b>                                   | Phase Ia - Schedule A: 0.2 mg BI 894999 | Phase Ia - Schedule A: 1 mg BI 894999 | Phase Ia - Schedule A: 1.5 mg BI 894999 |
|---|---|---------------------------------------|---|
| Total subjects affected by non-serious adverse events               |   |                                       |   |
| subjects affected / exposed   | 2 / 2 (100.00%)                         | 3 / 3 (100.00%)                       | 6 / 6 (100.00%)                         |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |   |                                       |   |
| Tumour pain   |   |                                       |   |
| subjects affected / exposed   | 0 / 2 (0.00%)                           | 0 / 3 (0.00%)                         | 0 / 6 (0.00%)                           |
| occurrences (all)   | 0                                       | 0                                     | 0                                       |
| Vascular disorders  |   |                                       |   |
| Hypotension   |   |                                       |   |
| subjects affected / exposed   | 0 / 2 (0.00%)                           | 0 / 3 (0.00%)                         | 0 / 6 (0.00%)                           |
| occurrences (all)   | 0                                       | 0                                     | 0                                       |
| Hypertension  |   |                                       |   |
| subjects affected / exposed   | 1 / 2 (50.00%)                          | 0 / 3 (0.00%)                         | 1 / 6 (16.67%)                          |
| occurrences (all)   | 1                                       | 0                                     | 2                                       |
| Haematoma   |   |                                       |   |
| subjects affected / exposed   | 0 / 2 (0.00%)                           | 0 / 3 (0.00%)                         | 0 / 6 (0.00%)                           |
| occurrences (all)   | 0                                       | 0                                     | 0                                       |
| Orthostatic hypotension   |   |                                       |   |
| subjects affected / exposed   | 0 / 2 (0.00%)                           | 0 / 3 (0.00%)                         | 0 / 6 (0.00%)                           |
| occurrences (all)   | 0                                       | 0                                     | 0                                       |
| Pallor  |   |                                       |   |
| subjects affected / exposed   | 0 / 2 (0.00%)                           | 0 / 3 (0.00%)                         | 0 / 6 (0.00%)                           |
| occurrences (all)   | 0                                       | 0                                     | 0                                       |
| General disorders and administration site conditions                |   |                                       |   |

|                                       |                 |                 |                |
|---------------------------------------|-----------------|-----------------|----------------|
| Chest discomfort                      |                 |                 |                |
| subjects affected / exposed           | 0 / 2 (0.00%)   | 0 / 3 (0.00%)   | 0 / 6 (0.00%)  |
| occurrences (all)                     | 0               | 0               | 0              |
| Asthenia                              |                 |                 |                |
| subjects affected / exposed           | 0 / 2 (0.00%)   | 0 / 3 (0.00%)   | 0 / 6 (0.00%)  |
| occurrences (all)                     | 0               | 0               | 0              |
| Chest pain                            |                 |                 |                |
| subjects affected / exposed           | 1 / 2 (50.00%)  | 1 / 3 (33.33%)  | 0 / 6 (0.00%)  |
| occurrences (all)                     | 1               | 1               | 0              |
| Fatigue                               |                 |                 |                |
| subjects affected / exposed           | 2 / 2 (100.00%) | 3 / 3 (100.00%) | 4 / 6 (66.67%) |
| occurrences (all)                     | 2               | 3               | 4              |
| Facial pain                           |                 |                 |                |
| subjects affected / exposed           | 0 / 2 (0.00%)   | 0 / 3 (0.00%)   | 0 / 6 (0.00%)  |
| occurrences (all)                     | 0               | 0               | 0              |
| Chills                                |                 |                 |                |
| subjects affected / exposed           | 0 / 2 (0.00%)   | 0 / 3 (0.00%)   | 0 / 6 (0.00%)  |
| occurrences (all)                     | 0               | 0               | 0              |
| Gait disturbance                      |                 |                 |                |
| subjects affected / exposed           | 0 / 2 (0.00%)   | 0 / 3 (0.00%)   | 0 / 6 (0.00%)  |
| occurrences (all)                     | 0               | 0               | 0              |
| General physical health deterioration |                 |                 |                |
| subjects affected / exposed           | 0 / 2 (0.00%)   | 0 / 3 (0.00%)   | 0 / 6 (0.00%)  |
| occurrences (all)                     | 0               | 0               | 0              |
| Generalised oedema                    |                 |                 |                |
| subjects affected / exposed           | 0 / 2 (0.00%)   | 0 / 3 (0.00%)   | 0 / 6 (0.00%)  |
| occurrences (all)                     | 0               | 0               | 0              |
| Malaise                               |                 |                 |                |
| subjects affected / exposed           | 0 / 2 (0.00%)   | 0 / 3 (0.00%)   | 0 / 6 (0.00%)  |
| occurrences (all)                     | 0               | 0               | 0              |
| Hypothermia                           |                 |                 |                |
| subjects affected / exposed           | 0 / 2 (0.00%)   | 0 / 3 (0.00%)   | 0 / 6 (0.00%)  |
| occurrences (all)                     | 0               | 0               | 0              |
| Oedema peripheral                     |                 |                 |                |
| subjects affected / exposed           | 0 / 2 (0.00%)   | 0 / 3 (0.00%)   | 0 / 6 (0.00%)  |
| occurrences (all)                     | 0               | 0               | 0              |

|  |                     |                    |                     |
|--|---------------------|--------------------|---------------------|
| Non-cardiac chest pain<br>subjects affected / exposed<br>occurrences (all)   | 0 / 2 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0 | 0 / 6 (0.00%)<br>0  |
| Pain<br>subjects affected / exposed<br>occurrences (all)   | 0 / 2 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0 | 0 / 6 (0.00%)<br>0  |
| Pyrexia<br>subjects affected / exposed<br>occurrences (all)  | 1 / 2 (50.00%)<br>1 | 0 / 3 (0.00%)<br>0 | 0 / 6 (0.00%)<br>0  |
| Peripheral swelling<br>subjects affected / exposed<br>occurrences (all)  | 0 / 2 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0 | 0 / 6 (0.00%)<br>0  |
| Immune system disorders<br>Hypersensitivity<br>subjects affected / exposed<br>occurrences (all)                      | 0 / 2 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0 | 0 / 6 (0.00%)<br>0  |
| Iodine allergy<br>subjects affected / exposed<br>occurrences (all)   | 0 / 2 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0 | 0 / 6 (0.00%)<br>0  |
| Reproductive system and breast disorders<br>Erectile dysfunction<br>subjects affected / exposed<br>occurrences (all) | 0 / 2 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0 | 1 / 6 (16.67%)<br>1 |
| Heavy menstrual bleeding<br>subjects affected / exposed<br>occurrences (all)   | 0 / 2 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0 | 0 / 6 (0.00%)<br>0  |
| Oedema genital<br>subjects affected / exposed<br>occurrences (all)   | 0 / 2 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0 | 0 / 6 (0.00%)<br>0  |
| Perineal pain<br>subjects affected / exposed<br>occurrences (all)  | 0 / 2 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0 | 0 / 6 (0.00%)<br>0  |
| Scrotal oedema<br>subjects affected / exposed<br>occurrences (all)   | 0 / 2 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0 | 0 / 6 (0.00%)<br>0  |
| Testicular pain  |                     |                    |                     |

|   |                 |                |                |
|---|-----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 2 (0.00%)   | 0 / 3 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                               | 0               | 0              | 0              |
| Vulvovaginal discomfort                         |                 |                |                |
| subjects affected / exposed                     | 0 / 2 (0.00%)   | 0 / 3 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                               | 0               | 0              | 0              |
| Vaginal haemorrhage                             |                 |                |                |
| subjects affected / exposed                     | 0 / 2 (0.00%)   | 0 / 3 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                               | 0               | 0              | 0              |
| Respiratory, thoracic and mediastinal disorders |                 |                |                |
| Atelectasis                                     |                 |                |                |
| subjects affected / exposed                     | 0 / 2 (0.00%)   | 0 / 3 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                               | 0               | 0              | 0              |
| Dysphonia                                       |                 |                |                |
| subjects affected / exposed                     | 0 / 2 (0.00%)   | 0 / 3 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                               | 0               | 0              | 0              |
| Cough   |                 |                |                |
| subjects affected / exposed                     | 2 / 2 (100.00%) | 0 / 3 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                               | 3               | 0              | 0              |
| Dyspnoea  |                 |                |                |
| subjects affected / exposed                     | 1 / 2 (50.00%)  | 1 / 3 (33.33%) | 1 / 6 (16.67%) |
| occurrences (all)                               | 1               | 1              | 1              |
| Dyspnoea exertional                             |                 |                |                |
| subjects affected / exposed                     | 0 / 2 (0.00%)   | 0 / 3 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                               | 0               | 0              | 0              |
| Epistaxis                                       |                 |                |                |
| subjects affected / exposed                     | 0 / 2 (0.00%)   | 1 / 3 (33.33%) | 1 / 6 (16.67%) |
| occurrences (all)                               | 0               | 1              | 1              |
| Laryngeal inflammation                          |                 |                |                |
| subjects affected / exposed                     | 0 / 2 (0.00%)   | 0 / 3 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                               | 0               | 0              | 0              |
| Haemoptysis                                     |                 |                |                |
| subjects affected / exposed                     | 0 / 2 (0.00%)   | 0 / 3 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                               | 0               | 0              | 0              |
| Nasal discomfort                                |                 |                |                |

|                              |               |                |                |
|------------------------------|---------------|----------------|----------------|
| subjects affected / exposed  | 0 / 2 (0.00%) | 0 / 3 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)            | 0             | 0              | 0              |
| Oropharyngeal pain           |               |                |                |
| subjects affected / exposed  | 0 / 2 (0.00%) | 0 / 3 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)            | 0             | 0              | 0              |
| Pharyngeal inflammation      |               |                |                |
| subjects affected / exposed  | 0 / 2 (0.00%) | 0 / 3 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)            | 0             | 0              | 0              |
| Pleural effusion             |               |                |                |
| subjects affected / exposed  | 0 / 2 (0.00%) | 0 / 3 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)            | 0             | 0              | 0              |
| Pleuritic pain               |               |                |                |
| subjects affected / exposed  | 0 / 2 (0.00%) | 0 / 3 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)            | 0             | 0              | 0              |
| Productive cough             |               |                |                |
| subjects affected / exposed  | 0 / 2 (0.00%) | 1 / 3 (33.33%) | 0 / 6 (0.00%)  |
| occurrences (all)            | 0             | 2              | 0              |
| Rhinorrhoea                  |               |                |                |
| subjects affected / exposed  | 0 / 2 (0.00%) | 0 / 3 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)            | 0             | 0              | 0              |
| Respiratory tract congestion |               |                |                |
| subjects affected / exposed  | 0 / 2 (0.00%) | 0 / 3 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)            | 0             | 0              | 0              |
| Wheezing                     |               |                |                |
| subjects affected / exposed  | 0 / 2 (0.00%) | 0 / 3 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)            | 0             | 0              | 0              |
| Psychiatric disorders        |               |                |                |
| Affective disorder           |               |                |                |
| subjects affected / exposed  | 0 / 2 (0.00%) | 0 / 3 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)            | 0             | 0              | 0              |
| Agitation                    |               |                |                |
| subjects affected / exposed  | 0 / 2 (0.00%) | 0 / 3 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)            | 0             | 0              | 0              |
| Anxiety                      |               |                |                |
| subjects affected / exposed  | 0 / 2 (0.00%) | 0 / 3 (0.00%)  | 1 / 6 (16.67%) |
| occurrences (all)            | 0             | 0              | 2              |



|   |               |               |               |
|---|---------------|---------------|---------------|
| Confusional state                               |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all)                               | 0             | 0             | 0             |
| Depression                                      |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all)                               | 0             | 0             | 0             |
| Insomnia  |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all)                               | 0             | 0             | 0             |
| Hallucination                                   |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all)                               | 0             | 0             | 0             |
| Personality change                              |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all)                               | 0             | 0             | 0             |
| Sleep disorder                                  |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all)                               | 0             | 0             | 0             |
| Investigations                                  |               |               |               |
| Activated partial thromboplastin time prolonged |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all)                               | 0             | 0             | 0             |
| Activated partial thromboplastin time shortened |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all)                               | 0             | 0             | 0             |
| Alanine aminotransferase increased              |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all)                               | 0             | 0             | 0             |
| Aspartate aminotransferase increased            |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all)                               | 0             | 0             | 0             |
| Blood alkaline phosphatase increased            |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all)                               | 0             | 0             | 0             |
| Blood antidiuretic hormone                      |               |               |               |

|  |               |               |                |
|--|---------------|---------------|----------------|
| decreased                              |               |               |                |
| subjects affected / exposed            | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)                      | 0             | 0             | 0              |
| Blood bilirubin increased              |               |               |                |
| subjects affected / exposed            | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)                      | 0             | 0             | 0              |
| Blood creatine phosphokinase increased |               |               |                |
| subjects affected / exposed            | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all)                      | 0             | 0             | 2              |
| Blood creatinine increased             |               |               |                |
| subjects affected / exposed            | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)                      | 0             | 0             | 0              |
| Blood magnesium decreased              |               |               |                |
| subjects affected / exposed            | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)                      | 0             | 0             | 0              |
| Blood glucose increased                |               |               |                |
| subjects affected / exposed            | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)                      | 0             | 0             | 0              |
| C-reactive protein increased           |               |               |                |
| subjects affected / exposed            | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)                      | 0             | 0             | 0              |
| Cardiac murmur                         |               |               |                |
| subjects affected / exposed            | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)                      | 0             | 0             | 0              |
| Cortisol increased                     |               |               |                |
| subjects affected / exposed            | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)                      | 0             | 0             | 0              |
| Echocardiogram abnormal                |               |               |                |
| subjects affected / exposed            | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)                      | 0             | 0             | 0              |
| Electrocardiogram PR prolongation      |               |               |                |
| subjects affected / exposed            | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)                      | 0             | 0             | 0              |
| Ejection fraction decreased            |               |               |                |

|  |               |               |                |
|--|---------------|---------------|----------------|
| subjects affected / exposed              | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)                        | 0             | 0             | 0              |
| Electrocardiogram ST segment elevation   |               |               |                |
| subjects affected / exposed              | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)                        | 0             | 0             | 0              |
| Gamma-glutamyltransferase increased      |               |               |                |
| subjects affected / exposed              | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)                        | 0             | 0             | 0              |
| Electrocardiogram T wave inversion       |               |               |                |
| subjects affected / exposed              | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)                        | 0             | 0             | 0              |
| International normalised ratio increased |               |               |                |
| subjects affected / exposed              | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)                        | 0             | 0             | 0              |
| Lymphocyte count decreased               |               |               |                |
| subjects affected / exposed              | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)                        | 0             | 0             | 0              |
| Neutrophil count decreased               |               |               |                |
| subjects affected / exposed              | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)                        | 0             | 0             | 0              |
| Platelet count decreased                 |               |               |                |
| subjects affected / exposed              | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all)                        | 0             | 0             | 1              |
| Prothrombin level decreased              |               |               |                |
| subjects affected / exposed              | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)                        | 0             | 0             | 0              |
| Troponin I increased                     |               |               |                |
| subjects affected / exposed              | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)                        | 0             | 0             | 0              |
| Troponin T increased                     |               |               |                |
| subjects affected / exposed              | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all)                        | 0             | 0             | 1              |
| Troponin increased                       |               |               |                |

|  |               |               |                |
|--|---------------|---------------|----------------|
| subjects affected / exposed                    | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)                              | 0             | 0             | 0              |
| Urine output decreased                         |               |               |                |
| subjects affected / exposed                    | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)                              | 0             | 0             | 0              |
| Weight decreased                               |               |               |                |
| subjects affected / exposed                    | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)                              | 0             | 0             | 0              |
| White blood cell count decreased               |               |               |                |
| subjects affected / exposed                    | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)                              | 0             | 0             | 0              |
| Injury, poisoning and procedural complications |               |               |                |
| Contusion                                      |               |               |                |
| subjects affected / exposed                    | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)                              | 0             | 0             | 0              |
| Face injury                                    |               |               |                |
| subjects affected / exposed                    | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)                              | 0             | 0             | 0              |
| Infusion related reaction                      |               |               |                |
| subjects affected / exposed                    | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)                              | 0             | 0             | 0              |
| Limb injury                                    |               |               |                |
| subjects affected / exposed                    | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)                              | 0             | 0             | 0              |
| Muscle rupture                                 |               |               |                |
| subjects affected / exposed                    | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all)                              | 0             | 0             | 1              |
| Overdose                                       |               |               |                |
| subjects affected / exposed                    | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)                              | 0             | 0             | 0              |
| Post procedural haematoma                      |               |               |                |
| subjects affected / exposed                    | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)                              | 0             | 0             | 0              |
| Skin abrasion                                  |               |               |                |

|                                  |               |               |                |
|----------------------------------|---------------|---------------|----------------|
| subjects affected / exposed      | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)                | 0             | 0             | 0              |
| Procedural pain                  |               |               |                |
| subjects affected / exposed      | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)                | 0             | 0             | 0              |
| Subcutaneous haematoma           |               |               |                |
| subjects affected / exposed      | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)                | 0             | 0             | 0              |
| Skin laceration                  |               |               |                |
| subjects affected / exposed      | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)                | 0             | 0             | 0              |
| Tongue injury                    |               |               |                |
| subjects affected / exposed      | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)                | 0             | 0             | 0              |
| Tooth fracture                   |               |               |                |
| subjects affected / exposed      | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)                | 0             | 0             | 0              |
| Urinary tract stoma complication |               |               |                |
| subjects affected / exposed      | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)                | 0             | 0             | 0              |
| Cardiac disorders                |               |               |                |
| Atrial fibrillation              |               |               |                |
| subjects affected / exposed      | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)                | 0             | 0             | 0              |
| Angina pectoris                  |               |               |                |
| subjects affected / exposed      | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)                | 0             | 0             | 0              |
| Palpitations                     |               |               |                |
| subjects affected / exposed      | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)                | 0             | 0             | 0              |
| Tachycardia                      |               |               |                |
| subjects affected / exposed      | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all)                | 0             | 0             | 1              |
| Sinus tachycardia                |               |               |                |
| subjects affected / exposed      | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)                | 0             | 0             | 0              |

|  |                     |                     |                    |
|--|---------------------|---------------------|--------------------|
| Ventricular arrhythmia<br>subjects affected / exposed<br>occurrences (all)   | 0 / 2 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0 |
| Nervous system disorders   |                     |                     |                    |
| Ageusia<br>subjects affected / exposed<br>occurrences (all)                  | 0 / 2 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0 |
| Agnosia<br>subjects affected / exposed<br>occurrences (all)                  | 0 / 2 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0 |
| Amnesia<br>subjects affected / exposed<br>occurrences (all)                  | 0 / 2 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0 |
| Cauda equina syndrome<br>subjects affected / exposed<br>occurrences (all)    | 0 / 2 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0 |
| Disturbance in attention<br>subjects affected / exposed<br>occurrences (all) | 0 / 2 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0 |
| Dizziness<br>subjects affected / exposed<br>occurrences (all)                | 0 / 2 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0 |
| Dizziness postural<br>subjects affected / exposed<br>occurrences (all)       | 0 / 2 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0 |
| Headache<br>subjects affected / exposed<br>occurrences (all)                 | 0 / 2 (0.00%)<br>0  | 1 / 3 (33.33%)<br>1 | 0 / 6 (0.00%)<br>0 |
| Dysgeusia<br>subjects affected / exposed<br>occurrences (all)                | 1 / 2 (50.00%)<br>1 | 0 / 3 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0 |
| Motor dysfunction<br>subjects affected / exposed<br>occurrences (all)        | 0 / 2 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0 |
| Neuropathy peripheral  |                     |                     |                    |

|                                      |               |               |                |
|--------------------------------------|---------------|---------------|----------------|
| subjects affected / exposed          | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)                    | 0             | 0             | 0              |
| Peripheral sensory neuropathy        |               |               |                |
| subjects affected / exposed          | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)                    | 0             | 0             | 0              |
| Paraesthesia                         |               |               |                |
| subjects affected / exposed          | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all)                    | 0             | 0             | 1              |
| Presyncope                           |               |               |                |
| subjects affected / exposed          | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)                    | 0             | 0             | 0              |
| Radiculopathy                        |               |               |                |
| subjects affected / exposed          | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)                    | 0             | 0             | 0              |
| Syncope                              |               |               |                |
| subjects affected / exposed          | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)                    | 0             | 0             | 0              |
| Somnolence                           |               |               |                |
| subjects affected / exposed          | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)                    | 0             | 0             | 0              |
| Sciatica                             |               |               |                |
| subjects affected / exposed          | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)                    | 0             | 0             | 0              |
| Taste disorder                       |               |               |                |
| subjects affected / exposed          | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all)                    | 0             | 0             | 1              |
| Blood and lymphatic system disorders |               |               |                |
| Anaemia                              |               |               |                |
| subjects affected / exposed          | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all)                    | 0             | 0             | 1              |
| Coagulopathy                         |               |               |                |
| subjects affected / exposed          | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)                    | 0             | 0             | 0              |
| Eosinophilia                         |               |               |                |
| subjects affected / exposed          | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)                    | 0             | 0             | 0              |

|  |                    |                     |                     |
|--|--------------------|---------------------|---------------------|
| Lymph node haemorrhage<br>subjects affected / exposed<br>occurrences (all)   | 0 / 2 (0.00%)<br>0 | 0 / 3 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  |
| Lymph node pain<br>subjects affected / exposed<br>occurrences (all)          | 0 / 2 (0.00%)<br>0 | 0 / 3 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  |
| Lymphadenopathy<br>subjects affected / exposed<br>occurrences (all)          | 0 / 2 (0.00%)<br>0 | 0 / 3 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  |
| Neutropenia<br>subjects affected / exposed<br>occurrences (all)              | 0 / 2 (0.00%)<br>0 | 0 / 3 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  |
| Lymphopenia<br>subjects affected / exposed<br>occurrences (all)              | 0 / 2 (0.00%)<br>0 | 0 / 3 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  |
| Thrombocytopenia<br>subjects affected / exposed<br>occurrences (all)         | 0 / 2 (0.00%)<br>0 | 1 / 3 (33.33%)<br>2 | 2 / 6 (33.33%)<br>3 |
| Ear and labyrinth disorders  |                    |                     |                     |
| Ear congestion<br>subjects affected / exposed<br>occurrences (all)           | 0 / 2 (0.00%)<br>0 | 0 / 3 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  |
| Ear haemorrhage<br>subjects affected / exposed<br>occurrences (all)          | 0 / 2 (0.00%)<br>0 | 0 / 3 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  |
| Ear pain<br>subjects affected / exposed<br>occurrences (all)                 | 0 / 2 (0.00%)<br>0 | 0 / 3 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  |
| Vertigo<br>subjects affected / exposed<br>occurrences (all)                  | 0 / 2 (0.00%)<br>0 | 0 / 3 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  |
| Eye disorders  |                    |                     |                     |
| Conjunctival haemorrhage<br>subjects affected / exposed<br>occurrences (all) | 0 / 2 (0.00%)<br>0 | 0 / 3 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  |
| Dry eye  |                    |                     |                     |



|                             |               |               |                |
|-----------------------------|---------------|---------------|----------------|
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)           | 0             | 0             | 0              |
| Vitreous haemorrhage        |               |               |                |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)           | 0             | 0             | 0              |
| Vision blurred              |               |               |                |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)           | 0             | 0             | 0              |
| Periorbital oedema          |               |               |                |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)           | 0             | 0             | 0              |
| Gastrointestinal disorders  |               |               |                |
| Abdominal pain upper        |               |               |                |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)           | 0             | 0             | 0              |
| Abdominal pain              |               |               |                |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all)           | 0             | 0             | 1              |
| Abdominal distension        |               |               |                |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)           | 0             | 0             | 0              |
| Anal fissure                |               |               |                |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)           | 0             | 0             | 0              |
| Anal haemorrhage            |               |               |                |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)           | 0             | 0             | 0              |
| Aphthous ulcer              |               |               |                |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)           | 0             | 0             | 0              |
| Angular cheilitis           |               |               |                |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)           | 0             | 0             | 0              |
| Anal inflammation           |               |               |                |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)           | 0             | 0             | 0              |

|                                  |               |               |                |
|----------------------------------|---------------|---------------|----------------|
| Ascites                          |               |               |                |
| subjects affected / exposed      | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all)                | 0             | 0             | 1              |
| Constipation                     |               |               |                |
| subjects affected / exposed      | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all)                | 0             | 0             | 1              |
| Diarrhoea                        |               |               |                |
| subjects affected / exposed      | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all)                | 0             | 0             | 3              |
| Dry mouth                        |               |               |                |
| subjects affected / exposed      | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)                | 0             | 0             | 0              |
| Dyspepsia                        |               |               |                |
| subjects affected / exposed      | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)                | 0             | 0             | 0              |
| Dysphagia                        |               |               |                |
| subjects affected / exposed      | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)                | 0             | 0             | 0              |
| Flatulence                       |               |               |                |
| subjects affected / exposed      | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)                | 0             | 0             | 0              |
| Gastritis                        |               |               |                |
| subjects affected / exposed      | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)                | 0             | 0             | 0              |
| Gastritis erosive                |               |               |                |
| subjects affected / exposed      | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)                | 0             | 0             | 0              |
| Gastrointestinal disorder        |               |               |                |
| subjects affected / exposed      | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)                | 0             | 0             | 0              |
| Gastrooesophageal reflux disease |               |               |                |
| subjects affected / exposed      | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)                | 0             | 0             | 0              |
| Haemorrhoids                     |               |               |                |
| subjects affected / exposed      | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)                | 0             | 0             | 0              |

|                                    |                |                |                |
|------------------------------------|----------------|----------------|----------------|
| Lip dry                            |                |                |                |
| subjects affected / exposed        | 0 / 2 (0.00%)  | 0 / 3 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                  | 0              | 0              | 0              |
| Melaena                            |                |                |                |
| subjects affected / exposed        | 0 / 2 (0.00%)  | 0 / 3 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                  | 0              | 0              | 0              |
| Lower gastrointestinal haemorrhage |                |                |                |
| subjects affected / exposed        | 0 / 2 (0.00%)  | 0 / 3 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                  | 0              | 0              | 0              |
| Nausea                             |                |                |                |
| subjects affected / exposed        | 0 / 2 (0.00%)  | 1 / 3 (33.33%) | 1 / 6 (16.67%) |
| occurrences (all)                  | 0              | 1              | 1              |
| Odynophagia                        |                |                |                |
| subjects affected / exposed        | 0 / 2 (0.00%)  | 0 / 3 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                  | 0              | 0              | 0              |
| Oral mucosal erythema              |                |                |                |
| subjects affected / exposed        | 0 / 2 (0.00%)  | 0 / 3 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                  | 0              | 0              | 0              |
| Retching                           |                |                |                |
| subjects affected / exposed        | 0 / 2 (0.00%)  | 0 / 3 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                  | 0              | 0              | 0              |
| Stomatitis                         |                |                |                |
| subjects affected / exposed        | 0 / 2 (0.00%)  | 0 / 3 (0.00%)  | 2 / 6 (33.33%) |
| occurrences (all)                  | 0              | 0              | 5              |
| Subileus                           |                |                |                |
| subjects affected / exposed        | 0 / 2 (0.00%)  | 0 / 3 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                  | 0              | 0              | 0              |
| Toothache                          |                |                |                |
| subjects affected / exposed        | 1 / 2 (50.00%) | 0 / 3 (0.00%)  | 1 / 6 (16.67%) |
| occurrences (all)                  | 1              | 0              | 1              |
| Vomiting                           |                |                |                |
| subjects affected / exposed        | 0 / 2 (0.00%)  | 1 / 3 (33.33%) | 1 / 6 (16.67%) |
| occurrences (all)                  | 0              | 5              | 1              |
| Hepatobiliary disorders            |                |                |                |
| Cholangitis                        |                |                |                |

|  |                |               |                |
|--|----------------|---------------|----------------|
| subjects affected / exposed            | 0 / 2 (0.00%)  | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)                      | 0              | 0             | 0              |
| Hepatic cytolysis                      |                |               |                |
| subjects affected / exposed            | 0 / 2 (0.00%)  | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)                      | 0              | 0             | 0              |
| Hepatic pain                           |                |               |                |
| subjects affected / exposed            | 0 / 2 (0.00%)  | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)                      | 0              | 0             | 0              |
| Skin and subcutaneous tissue disorders |                |               |                |
| Dermatitis psoriasiform                |                |               |                |
| subjects affected / exposed            | 0 / 2 (0.00%)  | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)                      | 0              | 0             | 0              |
| Dermatitis acneiform                   |                |               |                |
| subjects affected / exposed            | 0 / 2 (0.00%)  | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)                      | 0              | 0             | 0              |
| Dry skin                               |                |               |                |
| subjects affected / exposed            | 0 / 2 (0.00%)  | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)                      | 0              | 0             | 0              |
| Intertrigo                             |                |               |                |
| subjects affected / exposed            | 0 / 2 (0.00%)  | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)                      | 0              | 0             | 0              |
| Macule                                 |                |               |                |
| subjects affected / exposed            | 0 / 2 (0.00%)  | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)                      | 0              | 0             | 0              |
| Night sweats                           |                |               |                |
| subjects affected / exposed            | 0 / 2 (0.00%)  | 0 / 3 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all)                      | 0              | 0             | 1              |
| Eczema                                 |                |               |                |
| subjects affected / exposed            | 0 / 2 (0.00%)  | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)                      | 0              | 0             | 0              |
| Erythema                               |                |               |                |
| subjects affected / exposed            | 1 / 2 (50.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)                      | 1              | 0             | 0              |
| Prurigo                                |                |               |                |
| subjects affected / exposed            | 0 / 2 (0.00%)  | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)                      | 0              | 0             | 0              |

|                             |               |               |               |
|-----------------------------|---------------|---------------|---------------|
| Pruritus                    |               |               |               |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all)           | 0             | 0             | 0             |
| Psoriasis                   |               |               |               |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all)           | 0             | 0             | 0             |
| Petechiae                   |               |               |               |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all)           | 0             | 0             | 0             |
| Skin ulcer                  |               |               |               |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all)           | 0             | 0             | 0             |
| Rash                        |               |               |               |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all)           | 0             | 0             | 0             |
| Rash maculo-papular         |               |               |               |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all)           | 0             | 0             | 0             |
| Purpura                     |               |               |               |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all)           | 0             | 0             | 0             |
| Urticaria                   |               |               |               |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all)           | 0             | 0             | 0             |
| Renal and urinary disorders |               |               |               |
| Dysuria                     |               |               |               |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all)           | 0             | 0             | 0             |
| Haematuria                  |               |               |               |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all)           | 0             | 0             | 0             |
| Pollakiuria                 |               |               |               |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all)           | 0             | 0             | 0             |
| Urinary tract pain          |               |               |               |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 2 (0.00%)  | 0 / 3 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                               | 0              | 0              | 0              |
| Urinary retention                               |                |                |                |
| subjects affected / exposed                     | 0 / 2 (0.00%)  | 0 / 3 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                               | 0              | 0              | 0              |
| Renal failure                                   |                |                |                |
| subjects affected / exposed                     | 0 / 2 (0.00%)  | 0 / 3 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                               | 0              | 0              | 0              |
| Endocrine disorders                             |                |                |                |
| Hyperthyroidism                                 |                |                |                |
| subjects affected / exposed                     | 0 / 2 (0.00%)  | 0 / 3 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                               | 0              | 0              | 0              |
| Musculoskeletal and connective tissue disorders |                |                |                |
| Arthralgia                                      |                |                |                |
| subjects affected / exposed                     | 1 / 2 (50.00%) | 0 / 3 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                               | 1              | 0              | 0              |
| Back pain                                       |                |                |                |
| subjects affected / exposed                     | 0 / 2 (0.00%)  | 1 / 3 (33.33%) | 1 / 6 (16.67%) |
| occurrences (all)                               | 0              | 1              | 1              |
| Bone pain                                       |                |                |                |
| subjects affected / exposed                     | 0 / 2 (0.00%)  | 0 / 3 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                               | 0              | 0              | 0              |
| Flank pain                                      |                |                |                |
| subjects affected / exposed                     | 0 / 2 (0.00%)  | 0 / 3 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                               | 0              | 0              | 0              |
| Groin pain                                      |                |                |                |
| subjects affected / exposed                     | 0 / 2 (0.00%)  | 0 / 3 (0.00%)  | 1 / 6 (16.67%) |
| occurrences (all)                               | 0              | 0              | 1              |
| Muscular weakness                               |                |                |                |
| subjects affected / exposed                     | 0 / 2 (0.00%)  | 0 / 3 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                               | 0              | 0              | 0              |
| Muscle spasms                                   |                |                |                |
| subjects affected / exposed                     | 0 / 2 (0.00%)  | 0 / 3 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                               | 0              | 0              | 0              |
| Myalgia   |                |                |                |

|                               |               |               |                |
|-------------------------------|---------------|---------------|----------------|
| subjects affected / exposed   | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)             | 0             | 0             | 0              |
| Neck pain                     |               |               |                |
| subjects affected / exposed   | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)             | 0             | 0             | 0              |
| Pain in extremity             |               |               |                |
| subjects affected / exposed   | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)             | 0             | 0             | 0              |
| Pubic pain                    |               |               |                |
| subjects affected / exposed   | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)             | 0             | 0             | 0              |
| Infections and infestations   |               |               |                |
| Bronchitis                    |               |               |                |
| subjects affected / exposed   | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)             | 0             | 0             | 0              |
| Bronchitis viral              |               |               |                |
| subjects affected / exposed   | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)             | 0             | 0             | 0              |
| Clostridial infection         |               |               |                |
| subjects affected / exposed   | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)             | 0             | 0             | 0              |
| Clostridium difficile colitis |               |               |                |
| subjects affected / exposed   | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all)             | 0             | 0             | 1              |
| Conjunctivitis                |               |               |                |
| subjects affected / exposed   | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)             | 0             | 0             | 0              |
| Erysipelas                    |               |               |                |
| subjects affected / exposed   | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)             | 0             | 0             | 0              |
| Diverticulitis                |               |               |                |
| subjects affected / exposed   | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)             | 0             | 0             | 0              |
| Cystitis                      |               |               |                |
| subjects affected / exposed   | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)             | 0             | 0             | 0              |

|                                     |               |               |               |
|-------------------------------------|---------------|---------------|---------------|
| Gastroenteritis                     |               |               |               |
| subjects affected / exposed         | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all)                   | 0             | 0             | 0             |
| Folliculitis                        |               |               |               |
| subjects affected / exposed         | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all)                   | 0             | 0             | 0             |
| Escherichia urinary tract infection |               |               |               |
| subjects affected / exposed         | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all)                   | 0             | 0             | 0             |
| Genital herpes simplex              |               |               |               |
| subjects affected / exposed         | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all)                   | 0             | 0             | 0             |
| Genital infection fungal            |               |               |               |
| subjects affected / exposed         | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all)                   | 0             | 0             | 0             |
| Herpes dermatitis                   |               |               |               |
| subjects affected / exposed         | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all)                   | 0             | 0             | 0             |
| Impetigo                            |               |               |               |
| subjects affected / exposed         | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all)                   | 0             | 0             | 0             |
| Herpes zoster                       |               |               |               |
| subjects affected / exposed         | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all)                   | 0             | 0             | 0             |
| Influenza                           |               |               |               |
| subjects affected / exposed         | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all)                   | 0             | 0             | 0             |
| Infection                           |               |               |               |
| subjects affected / exposed         | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all)                   | 0             | 0             | 0             |
| Nasopharyngitis                     |               |               |               |
| subjects affected / exposed         | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all)                   | 0             | 0             | 0             |
| Oesophageal infection               |               |               |               |
| subjects affected / exposed         | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all)                   | 0             | 0             | 0             |



|                                       |               |               |                |
|---------------------------------------|---------------|---------------|----------------|
| Pharyngitis                           |               |               |                |
| subjects affected / exposed           | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)                     | 0             | 0             | 0              |
| Oral herpes                           |               |               |                |
| subjects affected / exposed           | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)                     | 0             | 0             | 0              |
| Pneumonia                             |               |               |                |
| subjects affected / exposed           | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)                     | 0             | 0             | 0              |
| Rash pustular                         |               |               |                |
| subjects affected / exposed           | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)                     | 0             | 0             | 0              |
| Respiratory tract infection           |               |               |                |
| subjects affected / exposed           | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)                     | 0             | 0             | 0              |
| Respiratory tract infection bacterial |               |               |                |
| subjects affected / exposed           | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)                     | 0             | 0             | 0              |
| Sinusitis                             |               |               |                |
| subjects affected / exposed           | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)                     | 0             | 0             | 0              |
| Tooth abscess                         |               |               |                |
| subjects affected / exposed           | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all)                     | 0             | 0             | 1              |
| Tooth infection                       |               |               |                |
| subjects affected / exposed           | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all)                     | 0             | 0             | 1              |
| Tracheitis                            |               |               |                |
| subjects affected / exposed           | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)                     | 0             | 0             | 0              |
| Upper respiratory tract infection     |               |               |                |
| subjects affected / exposed           | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all)                     | 0             | 0             | 1              |
| Urinary tract infection enterococcal  |               |               |                |
| subjects affected / exposed           | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)                     | 0             | 0             | 0              |

|                                    |                |                |                |
|------------------------------------|----------------|----------------|----------------|
| Urinary tract infection            |                |                |                |
| subjects affected / exposed        | 0 / 2 (0.00%)  | 0 / 3 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                  | 0              | 0              | 0              |
| Mucosal infection                  |                |                |                |
| subjects affected / exposed        | 0 / 2 (0.00%)  | 0 / 3 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                  | 0              | 0              | 0              |
| Stoma site infection               |                |                |                |
| subjects affected / exposed        | 0 / 2 (0.00%)  | 0 / 3 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                  | 0              | 0              | 0              |
| Metabolism and nutrition disorders |                |                |                |
| Acidosis                           |                |                |                |
| subjects affected / exposed        | 0 / 2 (0.00%)  | 0 / 3 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                  | 0              | 0              | 0              |
| Decreased appetite                 |                |                |                |
| subjects affected / exposed        | 1 / 2 (50.00%) | 1 / 3 (33.33%) | 3 / 6 (50.00%) |
| occurrences (all)                  | 1              | 1              | 3              |
| Cell death                         |                |                |                |
| subjects affected / exposed        | 0 / 2 (0.00%)  | 0 / 3 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                  | 0              | 0              | 0              |
| Dehydration                        |                |                |                |
| subjects affected / exposed        | 0 / 2 (0.00%)  | 0 / 3 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                  | 0              | 0              | 0              |
| Fluid retention                    |                |                |                |
| subjects affected / exposed        | 0 / 2 (0.00%)  | 0 / 3 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                  | 0              | 0              | 0              |
| Folate deficiency                  |                |                |                |
| subjects affected / exposed        | 0 / 2 (0.00%)  | 0 / 3 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                  | 0              | 0              | 0              |
| Gout                               |                |                |                |
| subjects affected / exposed        | 0 / 2 (0.00%)  | 0 / 3 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                  | 0              | 0              | 0              |
| Hypercalcaemia                     |                |                |                |
| subjects affected / exposed        | 0 / 2 (0.00%)  | 0 / 3 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                  | 0              | 0              | 0              |
| Hyperkalaemia                      |                |                |                |

|                             |                |               |                |
|-----------------------------|----------------|---------------|----------------|
| subjects affected / exposed | 0 / 2 (0.00%)  | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |
| Hyperglycaemia              |                |               |                |
| subjects affected / exposed | 0 / 2 (0.00%)  | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |
| Hyperphosphataemia          |                |               |                |
| subjects affected / exposed | 0 / 2 (0.00%)  | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |
| Hypoalbuminaemia            |                |               |                |
| subjects affected / exposed | 0 / 2 (0.00%)  | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |
| Hypocalcaemia               |                |               |                |
| subjects affected / exposed | 0 / 2 (0.00%)  | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |
| Hypokalaemia                |                |               |                |
| subjects affected / exposed | 0 / 2 (0.00%)  | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |
| Hypomagnesaemia             |                |               |                |
| subjects affected / exposed | 0 / 2 (0.00%)  | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |
| Hyponatraemia               |                |               |                |
| subjects affected / exposed | 0 / 2 (0.00%)  | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |
| Hypophosphataemia           |                |               |                |
| subjects affected / exposed | 1 / 2 (50.00%) | 0 / 3 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all)           | 2              | 0             | 1              |
| Malnutrition                |                |               |                |
| subjects affected / exposed | 0 / 2 (0.00%)  | 0 / 3 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0              |

| <b>Non-serious adverse events</b>                                   | Phase Ia - Schedule A: 2 mg BI 894999 | Phase Ia - Schedule C: 6/3 mg BI 894999 | Phase Ia - Schedule B: 1.5 mg BI 894999 |
|---|---------------------------------------|---|---|
| Total subjects affected by non-serious adverse events               |                                       |   |   |
| subjects affected / exposed   | 6 / 6 (100.00%)                       | 15 / 15 (100.00%)                       | 6 / 6 (100.00%)                         |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                                       |   |   |

|   |                     |                       |                     |
|---|---------------------|-----------------------|---------------------|
| Tumour pain<br>subjects affected / exposed<br>occurrences (all)             | 0 / 6 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0   | 0 / 6 (0.00%)<br>0  |
| Vascular disorders  |                     |                       |                     |
| Hypotension<br>subjects affected / exposed<br>occurrences (all)             | 0 / 6 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0   | 0 / 6 (0.00%)<br>0  |
| Hypertension<br>subjects affected / exposed<br>occurrences (all)            | 0 / 6 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0   | 0 / 6 (0.00%)<br>0  |
| Haematoma<br>subjects affected / exposed<br>occurrences (all)               | 0 / 6 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0   | 0 / 6 (0.00%)<br>0  |
| Orthostatic hypotension<br>subjects affected / exposed<br>occurrences (all) | 0 / 6 (0.00%)<br>0  | 1 / 15 (6.67%)<br>1   | 0 / 6 (0.00%)<br>0  |
| Pallor<br>subjects affected / exposed<br>occurrences (all)                  | 0 / 6 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0   | 0 / 6 (0.00%)<br>0  |
| General disorders and administration<br>site conditions                     |                     |                       |                     |
| Chest discomfort<br>subjects affected / exposed<br>occurrences (all)        | 0 / 6 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0   | 0 / 6 (0.00%)<br>0  |
| Asthenia<br>subjects affected / exposed<br>occurrences (all)                | 0 / 6 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0   | 1 / 6 (16.67%)<br>2 |
| Chest pain<br>subjects affected / exposed<br>occurrences (all)              | 0 / 6 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0   | 1 / 6 (16.67%)<br>1 |
| Fatigue<br>subjects affected / exposed<br>occurrences (all)                 | 4 / 6 (66.67%)<br>5 | 8 / 15 (53.33%)<br>10 | 1 / 6 (16.67%)<br>1 |
| Facial pain<br>subjects affected / exposed<br>occurrences (all)             | 0 / 6 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0   | 0 / 6 (0.00%)<br>0  |
| Chills  |                     |                       |                     |

|                                       |               |                |               |
|---------------------------------------|---------------|----------------|---------------|
| subjects affected / exposed           | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all)                     | 0             | 0              | 0             |
| Gait disturbance                      |               |                |               |
| subjects affected / exposed           | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all)                     | 0             | 0              | 0             |
| General physical health deterioration |               |                |               |
| subjects affected / exposed           | 0 / 6 (0.00%) | 1 / 15 (6.67%) | 0 / 6 (0.00%) |
| occurrences (all)                     | 0             | 1              | 0             |
| Generalised oedema                    |               |                |               |
| subjects affected / exposed           | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all)                     | 0             | 0              | 0             |
| Malaise                               |               |                |               |
| subjects affected / exposed           | 0 / 6 (0.00%) | 1 / 15 (6.67%) | 0 / 6 (0.00%) |
| occurrences (all)                     | 0             | 1              | 0             |
| Hypothermia                           |               |                |               |
| subjects affected / exposed           | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all)                     | 0             | 0              | 0             |
| Oedema peripheral                     |               |                |               |
| subjects affected / exposed           | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all)                     | 0             | 0              | 0             |
| Non-cardiac chest pain                |               |                |               |
| subjects affected / exposed           | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all)                     | 0             | 0              | 0             |
| Pain                                  |               |                |               |
| subjects affected / exposed           | 0 / 6 (0.00%) | 1 / 15 (6.67%) | 0 / 6 (0.00%) |
| occurrences (all)                     | 0             | 2              | 0             |
| Pyrexia                               |               |                |               |
| subjects affected / exposed           | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all)                     | 0             | 0              | 0             |
| Peripheral swelling                   |               |                |               |
| subjects affected / exposed           | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all)                     | 0             | 0              | 0             |
| Immune system disorders               |               |                |               |
| Hypersensitivity                      |               |                |               |
| subjects affected / exposed           | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all)                     | 0             | 0              | 0             |

|  |                    |                     |                     |
|--|--------------------|---------------------|---------------------|
| Iodine allergy<br>subjects affected / exposed<br>occurrences (all)           | 0 / 6 (0.00%)<br>0 | 0 / 15 (0.00%)<br>0 | 0 / 6 (0.00%)<br>0  |
| Reproductive system and breast disorders                                     |                    |                     |                     |
| Erectile dysfunction<br>subjects affected / exposed<br>occurrences (all)     | 0 / 6 (0.00%)<br>0 | 0 / 15 (0.00%)<br>0 | 0 / 6 (0.00%)<br>0  |
| Heavy menstrual bleeding<br>subjects affected / exposed<br>occurrences (all) | 0 / 6 (0.00%)<br>0 | 0 / 15 (0.00%)<br>0 | 0 / 6 (0.00%)<br>0  |
| Oedema genital<br>subjects affected / exposed<br>occurrences (all)           | 0 / 6 (0.00%)<br>0 | 0 / 15 (0.00%)<br>0 | 0 / 6 (0.00%)<br>0  |
| Perineal pain<br>subjects affected / exposed<br>occurrences (all)            | 0 / 6 (0.00%)<br>0 | 0 / 15 (0.00%)<br>0 | 0 / 6 (0.00%)<br>0  |
| Scrotal oedema<br>subjects affected / exposed<br>occurrences (all)           | 0 / 6 (0.00%)<br>0 | 0 / 15 (0.00%)<br>0 | 0 / 6 (0.00%)<br>0  |
| Testicular pain<br>subjects affected / exposed<br>occurrences (all)          | 0 / 6 (0.00%)<br>0 | 0 / 15 (0.00%)<br>0 | 0 / 6 (0.00%)<br>0  |
| Vulvovaginal discomfort<br>subjects affected / exposed<br>occurrences (all)  | 0 / 6 (0.00%)<br>0 | 1 / 15 (6.67%)<br>1 | 0 / 6 (0.00%)<br>0  |
| Vaginal haemorrhage<br>subjects affected / exposed<br>occurrences (all)      | 0 / 6 (0.00%)<br>0 | 1 / 15 (6.67%)<br>1 | 0 / 6 (0.00%)<br>0  |
| Respiratory, thoracic and mediastinal disorders                              |                    |                     |                     |
| Atelectasis<br>subjects affected / exposed<br>occurrences (all)              | 0 / 6 (0.00%)<br>0 | 0 / 15 (0.00%)<br>0 | 1 / 6 (16.67%)<br>1 |
| Dysphonia<br>subjects affected / exposed<br>occurrences (all)                | 0 / 6 (0.00%)<br>0 | 0 / 15 (0.00%)<br>0 | 0 / 6 (0.00%)<br>0  |
| Cough  |                    |                     |                     |

|                             |                |                 |                |
|-----------------------------|----------------|-----------------|----------------|
| subjects affected / exposed | 0 / 6 (0.00%)  | 3 / 15 (20.00%) | 0 / 6 (0.00%)  |
| occurrences (all)           | 0              | 3               | 0              |
| Dyspnoea                    |                |                 |                |
| subjects affected / exposed | 1 / 6 (16.67%) | 1 / 15 (6.67%)  | 0 / 6 (0.00%)  |
| occurrences (all)           | 1              | 1               | 0              |
| Dyspnoea exertional         |                |                 |                |
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  | 1 / 6 (16.67%) |
| occurrences (all)           | 0              | 0               | 1              |
| Epistaxis                   |                |                 |                |
| subjects affected / exposed | 0 / 6 (0.00%)  | 1 / 15 (6.67%)  | 0 / 6 (0.00%)  |
| occurrences (all)           | 0              | 1               | 0              |
| Laryngeal inflammation      |                |                 |                |
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)           | 0              | 0               | 0              |
| Haemoptysis                 |                |                 |                |
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)           | 0              | 0               | 0              |
| Nasal discomfort            |                |                 |                |
| subjects affected / exposed | 0 / 6 (0.00%)  | 1 / 15 (6.67%)  | 0 / 6 (0.00%)  |
| occurrences (all)           | 0              | 1               | 0              |
| Oropharyngeal pain          |                |                 |                |
| subjects affected / exposed | 0 / 6 (0.00%)  | 2 / 15 (13.33%) | 0 / 6 (0.00%)  |
| occurrences (all)           | 0              | 2               | 0              |
| Pharyngeal inflammation     |                |                 |                |
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)           | 0              | 0               | 0              |
| Pleural effusion            |                |                 |                |
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)           | 0              | 0               | 0              |
| Pleuritic pain              |                |                 |                |
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)           | 0              | 0               | 0              |
| Productive cough            |                |                 |                |
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)           | 0              | 0               | 0              |
| Rhinorrhoea                 |                |                 |                |

|                              |                |                 |               |
|------------------------------|----------------|-----------------|---------------|
| subjects affected / exposed  | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  | 0 / 6 (0.00%) |
| occurrences (all)            | 0              | 0               | 0             |
| Respiratory tract congestion |                |                 |               |
| subjects affected / exposed  | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  | 0 / 6 (0.00%) |
| occurrences (all)            | 0              | 0               | 0             |
| Wheezing                     |                |                 |               |
| subjects affected / exposed  | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  | 0 / 6 (0.00%) |
| occurrences (all)            | 0              | 0               | 0             |
| Psychiatric disorders        |                |                 |               |
| Affective disorder           |                |                 |               |
| subjects affected / exposed  | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  | 0 / 6 (0.00%) |
| occurrences (all)            | 0              | 0               | 0             |
| Agitation                    |                |                 |               |
| subjects affected / exposed  | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  | 0 / 6 (0.00%) |
| occurrences (all)            | 0              | 0               | 0             |
| Anxiety                      |                |                 |               |
| subjects affected / exposed  | 1 / 6 (16.67%) | 0 / 15 (0.00%)  | 0 / 6 (0.00%) |
| occurrences (all)            | 1              | 0               | 0             |
| Confusional state            |                |                 |               |
| subjects affected / exposed  | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  | 0 / 6 (0.00%) |
| occurrences (all)            | 0              | 0               | 0             |
| Depression                   |                |                 |               |
| subjects affected / exposed  | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  | 0 / 6 (0.00%) |
| occurrences (all)            | 0              | 0               | 0             |
| Insomnia                     |                |                 |               |
| subjects affected / exposed  | 0 / 6 (0.00%)  | 2 / 15 (13.33%) | 0 / 6 (0.00%) |
| occurrences (all)            | 0              | 2               | 0             |
| Hallucination                |                |                 |               |
| subjects affected / exposed  | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  | 0 / 6 (0.00%) |
| occurrences (all)            | 0              | 0               | 0             |
| Personality change           |                |                 |               |
| subjects affected / exposed  | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  | 0 / 6 (0.00%) |
| occurrences (all)            | 0              | 0               | 0             |
| Sleep disorder               |                |                 |               |
| subjects affected / exposed  | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  | 0 / 6 (0.00%) |
| occurrences (all)            | 0              | 0               | 0             |



|   |                |                 |                |
|---|----------------|-----------------|----------------|
| Investigations                                  |                |                 |                |
| Activated partial thromboplastin time prolonged |                |                 |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                               | 0              | 0               | 0              |
| Activated partial thromboplastin time shortened |                |                 |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                               | 0              | 0               | 0              |
| Alanine aminotransferase increased              |                |                 |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 1 / 15 (6.67%)  | 0 / 6 (0.00%)  |
| occurrences (all)                               | 0              | 1               | 0              |
| Aspartate aminotransferase increased            |                |                 |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 2 / 15 (13.33%) | 0 / 6 (0.00%)  |
| occurrences (all)                               | 0              | 2               | 0              |
| Blood alkaline phosphatase increased            |                |                 |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                               | 0              | 0               | 0              |
| Blood antidiuretic hormone decreased            |                |                 |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                               | 0              | 0               | 0              |
| Blood bilirubin increased                       |                |                 |                |
| subjects affected / exposed                     | 2 / 6 (33.33%) | 1 / 15 (6.67%)  | 1 / 6 (16.67%) |
| occurrences (all)                               | 2              | 2               | 3              |
| Blood creatine phosphokinase increased          |                |                 |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                               | 0              | 0               | 0              |
| Blood creatinine increased                      |                |                 |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 1 / 15 (6.67%)  | 0 / 6 (0.00%)  |
| occurrences (all)                               | 0              | 1               | 0              |
| Blood magnesium decreased                       |                |                 |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                               | 0              | 0               | 0              |
| Blood glucose increased                         |                |                 |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                               | 0              | 0               | 0              |

|   |                     |                      |                    |
|---|---------------------|----------------------|--------------------|
| C-reactive protein increased<br>subjects affected / exposed<br>occurrences (all)                | 0 / 6 (0.00%)<br>0  | 1 / 15 (6.67%)<br>1  | 0 / 6 (0.00%)<br>0 |
| Cardiac murmur<br>subjects affected / exposed<br>occurrences (all)                              | 0 / 6 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0 |
| Cortisol increased<br>subjects affected / exposed<br>occurrences (all)                          | 0 / 6 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0 |
| Echocardiogram abnormal<br>subjects affected / exposed<br>occurrences (all)                     | 0 / 6 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0 |
| Electrocardiogram PR prolongation<br>subjects affected / exposed<br>occurrences (all)           | 0 / 6 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0 |
| Ejection fraction decreased<br>subjects affected / exposed<br>occurrences (all)                 | 0 / 6 (0.00%)<br>0  | 2 / 15 (13.33%)<br>2 | 0 / 6 (0.00%)<br>0 |
| Electrocardiogram ST segment<br>elevation<br>subjects affected / exposed<br>occurrences (all)   | 0 / 6 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0 |
| Gamma-glutamyltransferase<br>increased<br>subjects affected / exposed<br>occurrences (all)      | 0 / 6 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0 |
| Electrocardiogram T wave inversion<br>subjects affected / exposed<br>occurrences (all)          | 1 / 6 (16.67%)<br>1 | 0 / 15 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0 |
| International normalised ratio<br>increased<br>subjects affected / exposed<br>occurrences (all) | 0 / 6 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0 |
| Lymphocyte count decreased<br>subjects affected / exposed<br>occurrences (all)                  | 1 / 6 (16.67%)<br>1 | 1 / 15 (6.67%)<br>1  | 0 / 6 (0.00%)<br>0 |
| Neutrophil count decreased  |                     |                      |                    |

|  |                     |                     |                     |
|--|---------------------|---------------------|---------------------|
| subjects affected / exposed<br>occurrences (all)                                     | 0 / 6 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0 | 0 / 6 (0.00%)<br>0  |
| Platelet count decreased<br>subjects affected / exposed<br>occurrences (all)         | 0 / 6 (0.00%)<br>0  | 1 / 15 (6.67%)<br>1 | 0 / 6 (0.00%)<br>0  |
| Prothrombin level decreased<br>subjects affected / exposed<br>occurrences (all)      | 0 / 6 (0.00%)<br>0  | 1 / 15 (6.67%)<br>2 | 0 / 6 (0.00%)<br>0  |
| Troponin I increased<br>subjects affected / exposed<br>occurrences (all)             | 0 / 6 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0 | 0 / 6 (0.00%)<br>0  |
| Troponin T increased<br>subjects affected / exposed<br>occurrences (all)             | 2 / 6 (33.33%)<br>4 | 1 / 15 (6.67%)<br>2 | 1 / 6 (16.67%)<br>1 |
| Troponin increased<br>subjects affected / exposed<br>occurrences (all)               | 0 / 6 (0.00%)<br>0  | 1 / 15 (6.67%)<br>1 | 0 / 6 (0.00%)<br>0  |
| Urine output decreased<br>subjects affected / exposed<br>occurrences (all)           | 0 / 6 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0 | 0 / 6 (0.00%)<br>0  |
| Weight decreased<br>subjects affected / exposed<br>occurrences (all)                 | 1 / 6 (16.67%)<br>1 | 0 / 15 (0.00%)<br>0 | 1 / 6 (16.67%)<br>1 |
| White blood cell count decreased<br>subjects affected / exposed<br>occurrences (all) | 0 / 6 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0 | 0 / 6 (0.00%)<br>0  |
| Injury, poisoning and procedural complications                                       |                     |                     |                     |
| Contusion<br>subjects affected / exposed<br>occurrences (all)                        | 0 / 6 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0 | 0 / 6 (0.00%)<br>0  |
| Face injury<br>subjects affected / exposed<br>occurrences (all)                      | 0 / 6 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0 | 0 / 6 (0.00%)<br>0  |
| Infusion related reaction  |                     |                     |                     |

|                                  |               |                |               |
|----------------------------------|---------------|----------------|---------------|
| subjects affected / exposed      | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all)                | 0             | 0              | 0             |
| Limb injury                      |               |                |               |
| subjects affected / exposed      | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all)                | 0             | 0              | 0             |
| Muscle rupture                   |               |                |               |
| subjects affected / exposed      | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all)                | 0             | 0              | 0             |
| Overdose                         |               |                |               |
| subjects affected / exposed      | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all)                | 0             | 0              | 0             |
| Post procedural haematoma        |               |                |               |
| subjects affected / exposed      | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all)                | 0             | 0              | 0             |
| Skin abrasion                    |               |                |               |
| subjects affected / exposed      | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all)                | 0             | 0              | 0             |
| Procedural pain                  |               |                |               |
| subjects affected / exposed      | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all)                | 0             | 0              | 0             |
| Subcutaneous haematoma           |               |                |               |
| subjects affected / exposed      | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all)                | 0             | 0              | 0             |
| Skin laceration                  |               |                |               |
| subjects affected / exposed      | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all)                | 0             | 0              | 0             |
| Tongue injury                    |               |                |               |
| subjects affected / exposed      | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all)                | 0             | 0              | 0             |
| Tooth fracture                   |               |                |               |
| subjects affected / exposed      | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all)                | 0             | 0              | 0             |
| Urinary tract stoma complication |               |                |               |
| subjects affected / exposed      | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all)                | 0             | 0              | 0             |
| Cardiac disorders                |               |                |               |

|                             |                |                |                |
|-----------------------------|----------------|----------------|----------------|
| Atrial fibrillation         |                |                |                |
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 15 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0              |
| Angina pectoris             |                |                |                |
| subjects affected / exposed | 0 / 6 (0.00%)  | 1 / 15 (6.67%) | 0 / 6 (0.00%)  |
| occurrences (all)           | 0              | 1              | 0              |
| Palpitations                |                |                |                |
| subjects affected / exposed | 0 / 6 (0.00%)  | 1 / 15 (6.67%) | 1 / 6 (16.67%) |
| occurrences (all)           | 0              | 1              | 1              |
| Tachycardia                 |                |                |                |
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 15 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0              |
| Sinus tachycardia           |                |                |                |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 15 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)           | 1              | 0              | 0              |
| Ventricular arrhythmia      |                |                |                |
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 15 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0              |
| Nervous system disorders    |                |                |                |
| Ageusia                     |                |                |                |
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 15 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0              |
| Agnosia                     |                |                |                |
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 15 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all)           | 0              | 0              | 1              |
| Amnesia                     |                |                |                |
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 15 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0              |
| Cauda equina syndrome       |                |                |                |
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 15 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0              |
| Disturbance in attention    |                |                |                |
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 15 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0              |
| Dizziness                   |                |                |                |

|                               |                |                |               |
|-------------------------------|----------------|----------------|---------------|
| subjects affected / exposed   | 0 / 6 (0.00%)  | 1 / 15 (6.67%) | 0 / 6 (0.00%) |
| occurrences (all)             | 0              | 1              | 0             |
| Dizziness postural            |                |                |               |
| subjects affected / exposed   | 0 / 6 (0.00%)  | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all)             | 0              | 0              | 0             |
| Headache                      |                |                |               |
| subjects affected / exposed   | 0 / 6 (0.00%)  | 1 / 15 (6.67%) | 0 / 6 (0.00%) |
| occurrences (all)             | 0              | 1              | 0             |
| Dysgeusia                     |                |                |               |
| subjects affected / exposed   | 2 / 6 (33.33%) | 1 / 15 (6.67%) | 0 / 6 (0.00%) |
| occurrences (all)             | 2              | 1              | 0             |
| Motor dysfunction             |                |                |               |
| subjects affected / exposed   | 0 / 6 (0.00%)  | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all)             | 0              | 0              | 0             |
| Neuropathy peripheral         |                |                |               |
| subjects affected / exposed   | 0 / 6 (0.00%)  | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all)             | 0              | 0              | 0             |
| Peripheral sensory neuropathy |                |                |               |
| subjects affected / exposed   | 0 / 6 (0.00%)  | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all)             | 0              | 0              | 0             |
| Paraesthesia                  |                |                |               |
| subjects affected / exposed   | 0 / 6 (0.00%)  | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all)             | 0              | 0              | 0             |
| Presyncope                    |                |                |               |
| subjects affected / exposed   | 0 / 6 (0.00%)  | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all)             | 0              | 0              | 0             |
| Radiculopathy                 |                |                |               |
| subjects affected / exposed   | 0 / 6 (0.00%)  | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all)             | 0              | 0              | 0             |
| Syncope                       |                |                |               |
| subjects affected / exposed   | 0 / 6 (0.00%)  | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all)             | 0              | 0              | 0             |
| Somnolence                    |                |                |               |
| subjects affected / exposed   | 0 / 6 (0.00%)  | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all)             | 0              | 0              | 0             |
| Sciatica                      |                |                |               |

|                                      |                |                 |                |
|--------------------------------------|----------------|-----------------|----------------|
| subjects affected / exposed          | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                    | 0              | 0               | 0              |
| Taste disorder                       |                |                 |                |
| subjects affected / exposed          | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  | 2 / 6 (33.33%) |
| occurrences (all)                    | 0              | 0               | 3              |
| Blood and lymphatic system disorders |                |                 |                |
| Anaemia                              |                |                 |                |
| subjects affected / exposed          | 1 / 6 (16.67%) | 5 / 15 (33.33%) | 2 / 6 (33.33%) |
| occurrences (all)                    | 1              | 7               | 4              |
| Coagulopathy                         |                |                 |                |
| subjects affected / exposed          | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                    | 0              | 0               | 0              |
| Eosinophilia                         |                |                 |                |
| subjects affected / exposed          | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                    | 0              | 0               | 0              |
| Lymph node haemorrhage               |                |                 |                |
| subjects affected / exposed          | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                    | 0              | 0               | 0              |
| Lymph node pain                      |                |                 |                |
| subjects affected / exposed          | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                    | 0              | 0               | 0              |
| Lymphadenopathy                      |                |                 |                |
| subjects affected / exposed          | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                    | 0              | 0               | 0              |
| Neutropenia                          |                |                 |                |
| subjects affected / exposed          | 2 / 6 (33.33%) | 0 / 15 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                    | 2              | 0               | 0              |
| Lymphopenia                          |                |                 |                |
| subjects affected / exposed          | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                    | 0              | 0               | 0              |
| Thrombocytopenia                     |                |                 |                |
| subjects affected / exposed          | 5 / 6 (83.33%) | 8 / 15 (53.33%) | 0 / 6 (0.00%)  |
| occurrences (all)                    | 8              | 10              | 0              |
| Ear and labyrinth disorders          |                |                 |                |
| Ear congestion                       |                |                 |                |

|  |                     |                     |                    |
|--|---------------------|---------------------|--------------------|
| subjects affected / exposed<br>occurrences (all)   | 0 / 6 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0 | 0 / 6 (0.00%)<br>0 |
| Ear haemorrhage<br>subjects affected / exposed<br>occurrences (all)                                    | 0 / 6 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0 | 0 / 6 (0.00%)<br>0 |
| Ear pain<br>subjects affected / exposed<br>occurrences (all)   | 0 / 6 (0.00%)<br>0  | 1 / 15 (6.67%)<br>1 | 0 / 6 (0.00%)<br>0 |
| Vertigo<br>subjects affected / exposed<br>occurrences (all)  | 0 / 6 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0 | 0 / 6 (0.00%)<br>0 |
| Eye disorders<br>Conjunctival haemorrhage<br>subjects affected / exposed<br>occurrences (all)          | 0 / 6 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0 | 0 / 6 (0.00%)<br>0 |
| Dry eye<br>subjects affected / exposed<br>occurrences (all)  | 0 / 6 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0 | 0 / 6 (0.00%)<br>0 |
| Vitreous haemorrhage<br>subjects affected / exposed<br>occurrences (all)                               | 0 / 6 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0 | 0 / 6 (0.00%)<br>0 |
| Vision blurred<br>subjects affected / exposed<br>occurrences (all)                                     | 0 / 6 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0 | 0 / 6 (0.00%)<br>0 |
| Periorbital oedema<br>subjects affected / exposed<br>occurrences (all)                                 | 0 / 6 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0 | 0 / 6 (0.00%)<br>0 |
| Gastrointestinal disorders<br>Abdominal pain upper<br>subjects affected / exposed<br>occurrences (all) | 0 / 6 (0.00%)<br>0  | 1 / 15 (6.67%)<br>1 | 0 / 6 (0.00%)<br>0 |
| Abdominal pain<br>subjects affected / exposed<br>occurrences (all)                                     | 1 / 6 (16.67%)<br>1 | 1 / 15 (6.67%)<br>1 | 0 / 6 (0.00%)<br>0 |
| Abdominal distension   |                     |                     |                    |



|                             |                |                 |                |
|-----------------------------|----------------|-----------------|----------------|
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)           | 0              | 0               | 0              |
| Anal fissure                |                |                 |                |
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)           | 0              | 0               | 0              |
| Anal haemorrhage            |                |                 |                |
| subjects affected / exposed | 0 / 6 (0.00%)  | 1 / 15 (6.67%)  | 0 / 6 (0.00%)  |
| occurrences (all)           | 0              | 1               | 0              |
| Aphthous ulcer              |                |                 |                |
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)           | 0              | 0               | 0              |
| Angular cheilitis           |                |                 |                |
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)           | 0              | 0               | 0              |
| Anal inflammation           |                |                 |                |
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)           | 0              | 0               | 0              |
| Ascites                     |                |                 |                |
| subjects affected / exposed | 1 / 6 (16.67%) | 1 / 15 (6.67%)  | 0 / 6 (0.00%)  |
| occurrences (all)           | 1              | 1               | 0              |
| Constipation                |                |                 |                |
| subjects affected / exposed | 0 / 6 (0.00%)  | 1 / 15 (6.67%)  | 1 / 6 (16.67%) |
| occurrences (all)           | 0              | 1               | 1              |
| Diarrhoea                   |                |                 |                |
| subjects affected / exposed | 0 / 6 (0.00%)  | 8 / 15 (53.33%) | 3 / 6 (50.00%) |
| occurrences (all)           | 0              | 9               | 3              |
| Dry mouth                   |                |                 |                |
| subjects affected / exposed | 0 / 6 (0.00%)  | 1 / 15 (6.67%)  | 0 / 6 (0.00%)  |
| occurrences (all)           | 0              | 1               | 0              |
| Dyspepsia                   |                |                 |                |
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)           | 0              | 0               | 0              |
| Dysphagia                   |                |                 |                |
| subjects affected / exposed | 0 / 6 (0.00%)  | 1 / 15 (6.67%)  | 0 / 6 (0.00%)  |
| occurrences (all)           | 0              | 1               | 0              |
| Flatulence                  |                |                 |                |

|                                    |                |                 |                |
|------------------------------------|----------------|-----------------|----------------|
| subjects affected / exposed        | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                  | 0              | 0               | 0              |
| Gastritis                          |                |                 |                |
| subjects affected / exposed        | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                  | 0              | 0               | 0              |
| Gastritis erosive                  |                |                 |                |
| subjects affected / exposed        | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                  | 0              | 0               | 0              |
| Gastrointestinal disorder          |                |                 |                |
| subjects affected / exposed        | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  | 1 / 6 (16.67%) |
| occurrences (all)                  | 0              | 0               | 1              |
| Gastrooesophageal reflux disease   |                |                 |                |
| subjects affected / exposed        | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                  | 0              | 0               | 0              |
| Haemorrhoids                       |                |                 |                |
| subjects affected / exposed        | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                  | 0              | 0               | 0              |
| Lip dry                            |                |                 |                |
| subjects affected / exposed        | 0 / 6 (0.00%)  | 1 / 15 (6.67%)  | 0 / 6 (0.00%)  |
| occurrences (all)                  | 0              | 1               | 0              |
| Melaena                            |                |                 |                |
| subjects affected / exposed        | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                  | 0              | 0               | 0              |
| Lower gastrointestinal haemorrhage |                |                 |                |
| subjects affected / exposed        | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                  | 0              | 0               | 0              |
| Nausea                             |                |                 |                |
| subjects affected / exposed        | 2 / 6 (33.33%) | 4 / 15 (26.67%) | 4 / 6 (66.67%) |
| occurrences (all)                  | 3              | 4               | 5              |
| Odynophagia                        |                |                 |                |
| subjects affected / exposed        | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                  | 0              | 0               | 0              |
| Oral mucosal erythema              |                |                 |                |
| subjects affected / exposed        | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                  | 0              | 0               | 0              |
| Retching                           |                |                 |                |

|  |                |                 |                |
|--|----------------|-----------------|----------------|
| subjects affected / exposed            | 0 / 6 (0.00%)  | 1 / 15 (6.67%)  | 0 / 6 (0.00%)  |
| occurrences (all)                      | 0              | 1               | 0              |
| Stomatitis                             |                |                 |                |
| subjects affected / exposed            | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  | 1 / 6 (16.67%) |
| occurrences (all)                      | 0              | 0               | 1              |
| Subileus                               |                |                 |                |
| subjects affected / exposed            | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                      | 0              | 0               | 0              |
| Toothache                              |                |                 |                |
| subjects affected / exposed            | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                      | 0              | 0               | 0              |
| Vomiting                               |                |                 |                |
| subjects affected / exposed            | 1 / 6 (16.67%) | 3 / 15 (20.00%) | 3 / 6 (50.00%) |
| occurrences (all)                      | 1              | 3               | 6              |
| Hepatobiliary disorders                |                |                 |                |
| Cholangitis                            |                |                 |                |
| subjects affected / exposed            | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                      | 0              | 0               | 0              |
| Hepatic cytolysis                      |                |                 |                |
| subjects affected / exposed            | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                      | 0              | 0               | 0              |
| Hepatic pain                           |                |                 |                |
| subjects affected / exposed            | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                      | 0              | 0               | 0              |
| Skin and subcutaneous tissue disorders |                |                 |                |
| Dermatitis psoriasiform                |                |                 |                |
| subjects affected / exposed            | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                      | 0              | 0               | 0              |
| Dermatitis acneiform                   |                |                 |                |
| subjects affected / exposed            | 0 / 6 (0.00%)  | 1 / 15 (6.67%)  | 0 / 6 (0.00%)  |
| occurrences (all)                      | 0              | 1               | 0              |
| Dry skin                               |                |                 |                |
| subjects affected / exposed            | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)                      | 0              | 0               | 0              |
| Intertrigo                             |                |                 |                |

|                             |               |                |               |
|-----------------------------|---------------|----------------|---------------|
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all)           | 0             | 0              | 0             |
| Macule                      |               |                |               |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all)           | 0             | 0              | 0             |
| Night sweats                |               |                |               |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all)           | 0             | 0              | 0             |
| Eczema                      |               |                |               |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 15 (6.67%) | 0 / 6 (0.00%) |
| occurrences (all)           | 0             | 1              | 0             |
| Erythema                    |               |                |               |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all)           | 0             | 0              | 0             |
| Prurigo                     |               |                |               |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all)           | 0             | 0              | 0             |
| Pruritus                    |               |                |               |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all)           | 0             | 0              | 0             |
| Psoriasis                   |               |                |               |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all)           | 0             | 0              | 0             |
| Petechiae                   |               |                |               |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all)           | 0             | 0              | 0             |
| Skin ulcer                  |               |                |               |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all)           | 0             | 0              | 0             |
| Rash                        |               |                |               |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 15 (6.67%) | 0 / 6 (0.00%) |
| occurrences (all)           | 0             | 1              | 0             |
| Rash maculo-papular         |               |                |               |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all)           | 0             | 0              | 0             |
| Purpura                     |               |                |               |

|   |                     |                     |                     |
|---|---------------------|---------------------|---------------------|
| subjects affected / exposed<br>occurrences (all)  | 0 / 6 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0 | 0 / 6 (0.00%)<br>0  |
| Urticaria<br>subjects affected / exposed<br>occurrences (all)   | 1 / 6 (16.67%)<br>1 | 1 / 15 (6.67%)<br>1 | 0 / 6 (0.00%)<br>0  |
| Renal and urinary disorders<br>Dysuria<br>subjects affected / exposed<br>occurrences (all)                        | 0 / 6 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0 | 0 / 6 (0.00%)<br>0  |
| Haematuria<br>subjects affected / exposed<br>occurrences (all)  | 0 / 6 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0 | 0 / 6 (0.00%)<br>0  |
| Pollakiuria<br>subjects affected / exposed<br>occurrences (all)   | 0 / 6 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0 | 0 / 6 (0.00%)<br>0  |
| Urinary tract pain<br>subjects affected / exposed<br>occurrences (all)  | 0 / 6 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0 | 0 / 6 (0.00%)<br>0  |
| Urinary retention<br>subjects affected / exposed<br>occurrences (all)   | 0 / 6 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0 | 0 / 6 (0.00%)<br>0  |
| Renal failure<br>subjects affected / exposed<br>occurrences (all)   | 0 / 6 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0 | 0 / 6 (0.00%)<br>0  |
| Endocrine disorders<br>Hyperthyroidism<br>subjects affected / exposed<br>occurrences (all)                        | 0 / 6 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0 | 0 / 6 (0.00%)<br>0  |
| Musculoskeletal and connective tissue disorders<br>Arthralgia<br>subjects affected / exposed<br>occurrences (all) | 0 / 6 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0 | 1 / 6 (16.67%)<br>1 |
| Back pain<br>subjects affected / exposed<br>occurrences (all)   | 0 / 6 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0 | 0 / 6 (0.00%)<br>0  |
| Bone pain   |                     |                     |                     |

|                             |               |                |                |
|-----------------------------|---------------|----------------|----------------|
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)           | 0             | 0              | 0              |
| Flank pain                  |               |                |                |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)           | 0             | 0              | 0              |
| Groin pain                  |               |                |                |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)           | 0             | 0              | 0              |
| Muscular weakness           |               |                |                |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)           | 0             | 0              | 0              |
| Muscle spasms               |               |                |                |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)           | 0             | 0              | 0              |
| Myalgia                     |               |                |                |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)           | 0             | 0              | 0              |
| Neck pain                   |               |                |                |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)           | 0             | 0              | 0              |
| Pain in extremity           |               |                |                |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)           | 0             | 0              | 0              |
| Pubic pain                  |               |                |                |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)           | 0             | 0              | 0              |
| Infections and infestations |               |                |                |
| Bronchitis                  |               |                |                |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all)           | 0             | 0              | 1              |
| Bronchitis viral            |               |                |                |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)           | 0             | 0              | 0              |
| Clostridial infection       |               |                |                |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)           | 0             | 0              | 0              |

|                                     |                |                |               |
|-------------------------------------|----------------|----------------|---------------|
| Clostridium difficile colitis       |                |                |               |
| subjects affected / exposed         | 1 / 6 (16.67%) | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all)                   | 1              | 0              | 0             |
| Conjunctivitis                      |                |                |               |
| subjects affected / exposed         | 0 / 6 (0.00%)  | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all)                   | 0              | 0              | 0             |
| Erysipelas                          |                |                |               |
| subjects affected / exposed         | 1 / 6 (16.67%) | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all)                   | 1              | 0              | 0             |
| Diverticulitis                      |                |                |               |
| subjects affected / exposed         | 0 / 6 (0.00%)  | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all)                   | 0              | 0              | 0             |
| Cystitis                            |                |                |               |
| subjects affected / exposed         | 0 / 6 (0.00%)  | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all)                   | 0              | 0              | 0             |
| Gastroenteritis                     |                |                |               |
| subjects affected / exposed         | 0 / 6 (0.00%)  | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all)                   | 0              | 0              | 0             |
| Folliculitis                        |                |                |               |
| subjects affected / exposed         | 0 / 6 (0.00%)  | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all)                   | 0              | 0              | 0             |
| Escherichia urinary tract infection |                |                |               |
| subjects affected / exposed         | 1 / 6 (16.67%) | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all)                   | 1              | 0              | 0             |
| Genital herpes simplex              |                |                |               |
| subjects affected / exposed         | 0 / 6 (0.00%)  | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all)                   | 0              | 0              | 0             |
| Genital infection fungal            |                |                |               |
| subjects affected / exposed         | 0 / 6 (0.00%)  | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all)                   | 0              | 0              | 0             |
| Herpes dermatitis                   |                |                |               |
| subjects affected / exposed         | 0 / 6 (0.00%)  | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all)                   | 0              | 0              | 0             |
| Impetigo                            |                |                |               |
| subjects affected / exposed         | 0 / 6 (0.00%)  | 0 / 15 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all)                   | 0              | 0              | 0             |

|                                       |               |                |                |
|---------------------------------------|---------------|----------------|----------------|
| Herpes zoster                         |               |                |                |
| subjects affected / exposed           | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)                     | 0             | 0              | 0              |
| Influenza                             |               |                |                |
| subjects affected / exposed           | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)                     | 0             | 0              | 0              |
| Infection                             |               |                |                |
| subjects affected / exposed           | 0 / 6 (0.00%) | 1 / 15 (6.67%) | 0 / 6 (0.00%)  |
| occurrences (all)                     | 0             | 1              | 0              |
| Nasopharyngitis                       |               |                |                |
| subjects affected / exposed           | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all)                     | 0             | 0              | 1              |
| Oesophageal infection                 |               |                |                |
| subjects affected / exposed           | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)                     | 0             | 0              | 0              |
| Pharyngitis                           |               |                |                |
| subjects affected / exposed           | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)                     | 0             | 0              | 0              |
| Oral herpes                           |               |                |                |
| subjects affected / exposed           | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)                     | 0             | 0              | 0              |
| Pneumonia                             |               |                |                |
| subjects affected / exposed           | 0 / 6 (0.00%) | 1 / 15 (6.67%) | 0 / 6 (0.00%)  |
| occurrences (all)                     | 0             | 1              | 0              |
| Rash pustular                         |               |                |                |
| subjects affected / exposed           | 0 / 6 (0.00%) | 1 / 15 (6.67%) | 0 / 6 (0.00%)  |
| occurrences (all)                     | 0             | 1              | 0              |
| Respiratory tract infection           |               |                |                |
| subjects affected / exposed           | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)                     | 0             | 0              | 0              |
| Respiratory tract infection bacterial |               |                |                |
| subjects affected / exposed           | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)                     | 0             | 0              | 0              |
| Sinusitis                             |               |                |                |
| subjects affected / exposed           | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)                     | 0             | 0              | 0              |



|  |                     |                      |                     |
|--|---------------------|----------------------|---------------------|
| Tooth abscess<br>subjects affected / exposed<br>occurrences (all)                                  | 0 / 6 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  |
| Tooth infection<br>subjects affected / exposed<br>occurrences (all)                                | 0 / 6 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  |
| Tracheitis<br>subjects affected / exposed<br>occurrences (all)                                     | 0 / 6 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  |
| Upper respiratory tract infection<br>subjects affected / exposed<br>occurrences (all)              | 0 / 6 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  |
| Urinary tract infection enterococcal<br>subjects affected / exposed<br>occurrences (all)           | 0 / 6 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  |
| Urinary tract infection<br>subjects affected / exposed<br>occurrences (all)                        | 1 / 6 (16.67%)<br>1 | 0 / 15 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  |
| Mucosal infection<br>subjects affected / exposed<br>occurrences (all)                              | 0 / 6 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  |
| Stoma site infection<br>subjects affected / exposed<br>occurrences (all)                           | 0 / 6 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  |
| Metabolism and nutrition disorders<br>Acidosis<br>subjects affected / exposed<br>occurrences (all) | 0 / 6 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0  | 0 / 6 (0.00%)<br>0  |
| Decreased appetite<br>subjects affected / exposed<br>occurrences (all)                             | 2 / 6 (33.33%)<br>2 | 4 / 15 (26.67%)<br>4 | 1 / 6 (16.67%)<br>1 |
| Cell death<br>subjects affected / exposed<br>occurrences (all)                                     | 0 / 6 (0.00%)<br>0  | 1 / 15 (6.67%)<br>1  | 0 / 6 (0.00%)<br>0  |
| Dehydration  |                     |                      |                     |

|                             |                |                 |                |
|-----------------------------|----------------|-----------------|----------------|
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)           | 0              | 0               | 0              |
| Fluid retention             |                |                 |                |
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)           | 0              | 0               | 0              |
| Folate deficiency           |                |                 |                |
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)           | 0              | 0               | 0              |
| Gout                        |                |                 |                |
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)           | 0              | 0               | 0              |
| Hypercalcaemia              |                |                 |                |
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)           | 0              | 0               | 0              |
| Hyperkalaemia               |                |                 |                |
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)           | 0              | 0               | 0              |
| Hyperglycaemia              |                |                 |                |
| subjects affected / exposed | 0 / 6 (0.00%)  | 2 / 15 (13.33%) | 0 / 6 (0.00%)  |
| occurrences (all)           | 0              | 2               | 0              |
| Hyperphosphataemia          |                |                 |                |
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)           | 0              | 0               | 0              |
| Hypoalbuminaemia            |                |                 |                |
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 15 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)           | 0              | 0               | 0              |
| Hypocalcaemia               |                |                 |                |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 15 (0.00%)  | 0 / 6 (0.00%)  |
| occurrences (all)           | 1              | 0               | 0              |
| Hypokalaemia                |                |                 |                |
| subjects affected / exposed | 1 / 6 (16.67%) | 3 / 15 (20.00%) | 1 / 6 (16.67%) |
| occurrences (all)           | 1              | 4               | 1              |
| Hypomagnesaemia             |                |                 |                |
| subjects affected / exposed | 1 / 6 (16.67%) | 2 / 15 (13.33%) | 1 / 6 (16.67%) |
| occurrences (all)           | 1              | 2               | 1              |
| Hyponatraemia               |                |                 |                |

|                             |               |                |                |
|-----------------------------|---------------|----------------|----------------|
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all)           | 0             | 0              | 1              |
| Hypophosphataemia           |               |                |                |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 15 (6.67%) | 2 / 6 (33.33%) |
| occurrences (all)           | 0             | 1              | 2              |
| Malnutrition                |               |                |                |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 15 (0.00%) | 0 / 6 (0.00%)  |
| occurrences (all)           | 0             | 0              | 0              |

| <b>Non-serious adverse events</b>                                   | Phase Ia - Schedule B: 2 mg BI 894999 | Phase Ia - Schedule B: 2.5 mg BI 894999 | Phase Ia - Schedule C: 5/2.5 mg BI 894999 |
|---|---------------------------------------|---|---|
| Total subjects affected by non-serious adverse events               |                                       |   |   |
| subjects affected / exposed   | 6 / 6 (100.00%)                       | 12 / 13 (92.31%)                        | 4 / 4 (100.00%)                           |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                                       |   |   |
| Tumour pain   |                                       |   |   |
| subjects affected / exposed   | 0 / 6 (0.00%)                         | 0 / 13 (0.00%)                          | 0 / 4 (0.00%)                             |
| occurrences (all)   | 0                                     | 0                                       | 0   |
| Vascular disorders  |                                       |   |   |
| Hypotension   |                                       |   |   |
| subjects affected / exposed   | 0 / 6 (0.00%)                         | 1 / 13 (7.69%)                          | 0 / 4 (0.00%)                             |
| occurrences (all)   | 0                                     | 1                                       | 0   |
| Hypertension  |                                       |   |   |
| subjects affected / exposed   | 1 / 6 (16.67%)                        | 2 / 13 (15.38%)                         | 2 / 4 (50.00%)                            |
| occurrences (all)   | 3                                     | 2                                       | 2   |
| Haematoma   |                                       |   |   |
| subjects affected / exposed   | 0 / 6 (0.00%)                         | 1 / 13 (7.69%)                          | 0 / 4 (0.00%)                             |
| occurrences (all)   | 0                                     | 1                                       | 0   |
| Orthostatic hypotension   |                                       |   |   |
| subjects affected / exposed   | 0 / 6 (0.00%)                         | 0 / 13 (0.00%)                          | 0 / 4 (0.00%)                             |
| occurrences (all)   | 0                                     | 0                                       | 0   |
| Pallor  |                                       |   |   |
| subjects affected / exposed   | 0 / 6 (0.00%)                         | 1 / 13 (7.69%)                          | 0 / 4 (0.00%)                             |
| occurrences (all)   | 0                                     | 1                                       | 0   |
| General disorders and administration site conditions                |                                       |   |   |
| Chest discomfort  |                                       |   |   |

|                                       |                |                 |                |
|---------------------------------------|----------------|-----------------|----------------|
| subjects affected / exposed           | 0 / 6 (0.00%)  | 1 / 13 (7.69%)  | 0 / 4 (0.00%)  |
| occurrences (all)                     | 0              | 1               | 0              |
| Asthenia                              |                |                 |                |
| subjects affected / exposed           | 0 / 6 (0.00%)  | 1 / 13 (7.69%)  | 0 / 4 (0.00%)  |
| occurrences (all)                     | 0              | 1               | 0              |
| Chest pain                            |                |                 |                |
| subjects affected / exposed           | 0 / 6 (0.00%)  | 0 / 13 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                     | 0              | 0               | 0              |
| Fatigue                               |                |                 |                |
| subjects affected / exposed           | 3 / 6 (50.00%) | 6 / 13 (46.15%) | 2 / 4 (50.00%) |
| occurrences (all)                     | 4              | 10              | 4              |
| Facial pain                           |                |                 |                |
| subjects affected / exposed           | 0 / 6 (0.00%)  | 0 / 13 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                     | 0              | 0               | 0              |
| Chills                                |                |                 |                |
| subjects affected / exposed           | 0 / 6 (0.00%)  | 0 / 13 (0.00%)  | 1 / 4 (25.00%) |
| occurrences (all)                     | 0              | 0               | 1              |
| Gait disturbance                      |                |                 |                |
| subjects affected / exposed           | 0 / 6 (0.00%)  | 0 / 13 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                     | 0              | 0               | 0              |
| General physical health deterioration |                |                 |                |
| subjects affected / exposed           | 0 / 6 (0.00%)  | 0 / 13 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                     | 0              | 0               | 0              |
| Generalised oedema                    |                |                 |                |
| subjects affected / exposed           | 0 / 6 (0.00%)  | 0 / 13 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                     | 0              | 0               | 0              |
| Malaise                               |                |                 |                |
| subjects affected / exposed           | 0 / 6 (0.00%)  | 1 / 13 (7.69%)  | 0 / 4 (0.00%)  |
| occurrences (all)                     | 0              | 1               | 0              |
| Hypothermia                           |                |                 |                |
| subjects affected / exposed           | 0 / 6 (0.00%)  | 0 / 13 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                     | 0              | 0               | 0              |
| Oedema peripheral                     |                |                 |                |
| subjects affected / exposed           | 0 / 6 (0.00%)  | 3 / 13 (23.08%) | 0 / 4 (0.00%)  |
| occurrences (all)                     | 0              | 4               | 0              |
| Non-cardiac chest pain                |                |                 |                |

|  |                     |                      |                     |
|--|---------------------|----------------------|---------------------|
| subjects affected / exposed<br>occurrences (all) | 0 / 6 (0.00%)<br>0  | 0 / 13 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0  |
| Pain   |                     |                      |                     |
| subjects affected / exposed<br>occurrences (all) | 0 / 6 (0.00%)<br>0  | 0 / 13 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0  |
| Pyrexia  |                     |                      |                     |
| subjects affected / exposed<br>occurrences (all) | 1 / 6 (16.67%)<br>1 | 2 / 13 (15.38%)<br>2 | 1 / 4 (25.00%)<br>1 |
| Peripheral swelling                              |                     |                      |                     |
| subjects affected / exposed<br>occurrences (all) | 0 / 6 (0.00%)<br>0  | 0 / 13 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0  |
| Immune system disorders                          |                     |                      |                     |
| Hypersensitivity                                 |                     |                      |                     |
| subjects affected / exposed<br>occurrences (all) | 0 / 6 (0.00%)<br>0  | 0 / 13 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0  |
| Iodine allergy                                   |                     |                      |                     |
| subjects affected / exposed<br>occurrences (all) | 0 / 6 (0.00%)<br>0  | 1 / 13 (7.69%)<br>1  | 0 / 4 (0.00%)<br>0  |
| Reproductive system and breast disorders         |                     |                      |                     |
| Erectile dysfunction                             |                     |                      |                     |
| subjects affected / exposed<br>occurrences (all) | 0 / 6 (0.00%)<br>0  | 0 / 13 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0  |
| Heavy menstrual bleeding                         |                     |                      |                     |
| subjects affected / exposed<br>occurrences (all) | 0 / 6 (0.00%)<br>0  | 0 / 13 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0  |
| Oedema genital                                   |                     |                      |                     |
| subjects affected / exposed<br>occurrences (all) | 0 / 6 (0.00%)<br>0  | 0 / 13 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0  |
| Perineal pain                                    |                     |                      |                     |
| subjects affected / exposed<br>occurrences (all) | 0 / 6 (0.00%)<br>0  | 0 / 13 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0  |
| Scrotal oedema                                   |                     |                      |                     |
| subjects affected / exposed<br>occurrences (all) | 0 / 6 (0.00%)<br>0  | 0 / 13 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0  |
| Testicular pain                                  |                     |                      |                     |

|   |                |                 |                |
|---|----------------|-----------------|----------------|
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 13 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                               | 0              | 0               | 0              |
| Vulvovaginal discomfort                         |                |                 |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 13 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                               | 0              | 0               | 0              |
| Vaginal haemorrhage                             |                |                 |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 13 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                               | 0              | 0               | 0              |
| Respiratory, thoracic and mediastinal disorders |                |                 |                |
| Atelectasis                                     |                |                 |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 13 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                               | 0              | 0               | 0              |
| Dysphonia                                       |                |                 |                |
| subjects affected / exposed                     | 1 / 6 (16.67%) | 1 / 13 (7.69%)  | 0 / 4 (0.00%)  |
| occurrences (all)                               | 1              | 1               | 0              |
| Cough   |                |                 |                |
| subjects affected / exposed                     | 1 / 6 (16.67%) | 3 / 13 (23.08%) | 1 / 4 (25.00%) |
| occurrences (all)                               | 1              | 4               | 1              |
| Dyspnoea  |                |                 |                |
| subjects affected / exposed                     | 1 / 6 (16.67%) | 5 / 13 (38.46%) | 1 / 4 (25.00%) |
| occurrences (all)                               | 2              | 5               | 1              |
| Dyspnoea exertional                             |                |                 |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 13 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                               | 0              | 0               | 0              |
| Epistaxis                                       |                |                 |                |
| subjects affected / exposed                     | 1 / 6 (16.67%) | 0 / 13 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                               | 1              | 0               | 0              |
| Laryngeal inflammation                          |                |                 |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 13 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                               | 0              | 0               | 0              |
| Haemoptysis                                     |                |                 |                |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 13 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                               | 0              | 0               | 0              |
| Nasal discomfort                                |                |                 |                |

|                              |                |                 |               |
|------------------------------|----------------|-----------------|---------------|
| subjects affected / exposed  | 0 / 6 (0.00%)  | 0 / 13 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)            | 0              | 0               | 0             |
| Oropharyngeal pain           |                |                 |               |
| subjects affected / exposed  | 0 / 6 (0.00%)  | 0 / 13 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)            | 0              | 0               | 0             |
| Pharyngeal inflammation      |                |                 |               |
| subjects affected / exposed  | 0 / 6 (0.00%)  | 0 / 13 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)            | 0              | 0               | 0             |
| Pleural effusion             |                |                 |               |
| subjects affected / exposed  | 0 / 6 (0.00%)  | 2 / 13 (15.38%) | 0 / 4 (0.00%) |
| occurrences (all)            | 0              | 2               | 0             |
| Pleuritic pain               |                |                 |               |
| subjects affected / exposed  | 0 / 6 (0.00%)  | 0 / 13 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)            | 0              | 0               | 0             |
| Productive cough             |                |                 |               |
| subjects affected / exposed  | 0 / 6 (0.00%)  | 0 / 13 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)            | 0              | 0               | 0             |
| Rhinorrhoea                  |                |                 |               |
| subjects affected / exposed  | 0 / 6 (0.00%)  | 0 / 13 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)            | 0              | 0               | 0             |
| Respiratory tract congestion |                |                 |               |
| subjects affected / exposed  | 0 / 6 (0.00%)  | 1 / 13 (7.69%)  | 0 / 4 (0.00%) |
| occurrences (all)            | 0              | 1               | 0             |
| Wheezing                     |                |                 |               |
| subjects affected / exposed  | 1 / 6 (16.67%) | 0 / 13 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)            | 1              | 0               | 0             |
| Psychiatric disorders        |                |                 |               |
| Affective disorder           |                |                 |               |
| subjects affected / exposed  | 0 / 6 (0.00%)  | 0 / 13 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)            | 0              | 0               | 0             |
| Agitation                    |                |                 |               |
| subjects affected / exposed  | 0 / 6 (0.00%)  | 0 / 13 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)            | 0              | 0               | 0             |
| Anxiety                      |                |                 |               |
| subjects affected / exposed  | 0 / 6 (0.00%)  | 1 / 13 (7.69%)  | 0 / 4 (0.00%) |
| occurrences (all)            | 0              | 1               | 0             |

|   |               |                |                |
|---|---------------|----------------|----------------|
| Confusional state                               |               |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 13 (0.00%) | 0 / 4 (0.00%)  |
| occurrences (all)                               | 0             | 0              | 0              |
| Depression                                      |               |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 13 (0.00%) | 0 / 4 (0.00%)  |
| occurrences (all)                               | 0             | 0              | 0              |
| Insomnia  |               |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 13 (0.00%) | 1 / 4 (25.00%) |
| occurrences (all)                               | 0             | 0              | 1              |
| Hallucination                                   |               |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 1 / 13 (7.69%) | 0 / 4 (0.00%)  |
| occurrences (all)                               | 0             | 1              | 0              |
| Personality change                              |               |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 1 / 13 (7.69%) | 0 / 4 (0.00%)  |
| occurrences (all)                               | 0             | 1              | 0              |
| Sleep disorder                                  |               |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 13 (0.00%) | 0 / 4 (0.00%)  |
| occurrences (all)                               | 0             | 0              | 0              |
| Investigations                                  |               |                |                |
| Activated partial thromboplastin time prolonged |               |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 13 (0.00%) | 0 / 4 (0.00%)  |
| occurrences (all)                               | 0             | 0              | 0              |
| Activated partial thromboplastin time shortened |               |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 13 (0.00%) | 0 / 4 (0.00%)  |
| occurrences (all)                               | 0             | 0              | 0              |
| Alanine aminotransferase increased              |               |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 1 / 13 (7.69%) | 0 / 4 (0.00%)  |
| occurrences (all)                               | 0             | 2              | 0              |
| Aspartate aminotransferase increased            |               |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 0 / 13 (0.00%) | 0 / 4 (0.00%)  |
| occurrences (all)                               | 0             | 0              | 0              |
| Blood alkaline phosphatase increased            |               |                |                |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 1 / 13 (7.69%) | 0 / 4 (0.00%)  |
| occurrences (all)                               | 0             | 1              | 0              |
| Blood antidiuretic hormone                      |               |                |                |



|  |                |                |                |
|--|----------------|----------------|----------------|
| decreased                              |                |                |                |
| subjects affected / exposed            | 0 / 6 (0.00%)  | 0 / 13 (0.00%) | 0 / 4 (0.00%)  |
| occurrences (all)                      | 0              | 0              | 0              |
| Blood bilirubin increased              |                |                |                |
| subjects affected / exposed            | 0 / 6 (0.00%)  | 0 / 13 (0.00%) | 0 / 4 (0.00%)  |
| occurrences (all)                      | 0              | 0              | 0              |
| Blood creatine phosphokinase increased |                |                |                |
| subjects affected / exposed            | 1 / 6 (16.67%) | 1 / 13 (7.69%) | 1 / 4 (25.00%) |
| occurrences (all)                      | 4              | 1              | 1              |
| Blood creatinine increased             |                |                |                |
| subjects affected / exposed            | 0 / 6 (0.00%)  | 0 / 13 (0.00%) | 0 / 4 (0.00%)  |
| occurrences (all)                      | 0              | 0              | 0              |
| Blood magnesium decreased              |                |                |                |
| subjects affected / exposed            | 0 / 6 (0.00%)  | 0 / 13 (0.00%) | 0 / 4 (0.00%)  |
| occurrences (all)                      | 0              | 0              | 0              |
| Blood glucose increased                |                |                |                |
| subjects affected / exposed            | 0 / 6 (0.00%)  | 0 / 13 (0.00%) | 0 / 4 (0.00%)  |
| occurrences (all)                      | 0              | 0              | 0              |
| C-reactive protein increased           |                |                |                |
| subjects affected / exposed            | 0 / 6 (0.00%)  | 0 / 13 (0.00%) | 0 / 4 (0.00%)  |
| occurrences (all)                      | 0              | 0              | 0              |
| Cardiac murmur                         |                |                |                |
| subjects affected / exposed            | 0 / 6 (0.00%)  | 0 / 13 (0.00%) | 0 / 4 (0.00%)  |
| occurrences (all)                      | 0              | 0              | 0              |
| Cortisol increased                     |                |                |                |
| subjects affected / exposed            | 0 / 6 (0.00%)  | 0 / 13 (0.00%) | 0 / 4 (0.00%)  |
| occurrences (all)                      | 0              | 0              | 0              |
| Echocardiogram abnormal                |                |                |                |
| subjects affected / exposed            | 0 / 6 (0.00%)  | 0 / 13 (0.00%) | 0 / 4 (0.00%)  |
| occurrences (all)                      | 0              | 0              | 0              |
| Electrocardiogram PR prolongation      |                |                |                |
| subjects affected / exposed            | 0 / 6 (0.00%)  | 0 / 13 (0.00%) | 0 / 4 (0.00%)  |
| occurrences (all)                      | 0              | 0              | 0              |
| Ejection fraction decreased            |                |                |                |

|  |                |                 |                |
|--|----------------|-----------------|----------------|
| subjects affected / exposed              | 0 / 6 (0.00%)  | 1 / 13 (7.69%)  | 0 / 4 (0.00%)  |
| occurrences (all)                        | 0              | 1               | 0              |
| Electrocardiogram ST segment elevation   |                |                 |                |
| subjects affected / exposed              | 0 / 6 (0.00%)  | 1 / 13 (7.69%)  | 0 / 4 (0.00%)  |
| occurrences (all)                        | 0              | 1               | 0              |
| Gamma-glutamyltransferase increased      |                |                 |                |
| subjects affected / exposed              | 0 / 6 (0.00%)  | 1 / 13 (7.69%)  | 0 / 4 (0.00%)  |
| occurrences (all)                        | 0              | 1               | 0              |
| Electrocardiogram T wave inversion       |                |                 |                |
| subjects affected / exposed              | 0 / 6 (0.00%)  | 0 / 13 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                        | 0              | 0               | 0              |
| International normalised ratio increased |                |                 |                |
| subjects affected / exposed              | 0 / 6 (0.00%)  | 1 / 13 (7.69%)  | 0 / 4 (0.00%)  |
| occurrences (all)                        | 0              | 1               | 0              |
| Lymphocyte count decreased               |                |                 |                |
| subjects affected / exposed              | 0 / 6 (0.00%)  | 0 / 13 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                        | 0              | 0               | 0              |
| Neutrophil count decreased               |                |                 |                |
| subjects affected / exposed              | 0 / 6 (0.00%)  | 0 / 13 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                        | 0              | 0               | 0              |
| Platelet count decreased                 |                |                 |                |
| subjects affected / exposed              | 0 / 6 (0.00%)  | 1 / 13 (7.69%)  | 0 / 4 (0.00%)  |
| occurrences (all)                        | 0              | 1               | 0              |
| Prothrombin level decreased              |                |                 |                |
| subjects affected / exposed              | 0 / 6 (0.00%)  | 0 / 13 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                        | 0              | 0               | 0              |
| Troponin I increased                     |                |                 |                |
| subjects affected / exposed              | 0 / 6 (0.00%)  | 0 / 13 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                        | 0              | 0               | 0              |
| Troponin T increased                     |                |                 |                |
| subjects affected / exposed              | 1 / 6 (16.67%) | 2 / 13 (15.38%) | 2 / 4 (50.00%) |
| occurrences (all)                        | 1              | 2               | 3              |
| Troponin increased                       |                |                 |                |

|  |                |                |                |
|--|----------------|----------------|----------------|
| subjects affected / exposed                    | 0 / 6 (0.00%)  | 1 / 13 (7.69%) | 0 / 4 (0.00%)  |
| occurrences (all)                              | 0              | 1              | 0              |
| Urine output decreased                         |                |                |                |
| subjects affected / exposed                    | 0 / 6 (0.00%)  | 1 / 13 (7.69%) | 0 / 4 (0.00%)  |
| occurrences (all)                              | 0              | 2              | 0              |
| Weight decreased                               |                |                |                |
| subjects affected / exposed                    | 1 / 6 (16.67%) | 1 / 13 (7.69%) | 2 / 4 (50.00%) |
| occurrences (all)                              | 1              | 1              | 2              |
| White blood cell count decreased               |                |                |                |
| subjects affected / exposed                    | 0 / 6 (0.00%)  | 0 / 13 (0.00%) | 0 / 4 (0.00%)  |
| occurrences (all)                              | 0              | 0              | 0              |
| Injury, poisoning and procedural complications |                |                |                |
| Contusion                                      |                |                |                |
| subjects affected / exposed                    | 0 / 6 (0.00%)  | 0 / 13 (0.00%) | 0 / 4 (0.00%)  |
| occurrences (all)                              | 0              | 0              | 0              |
| Face injury                                    |                |                |                |
| subjects affected / exposed                    | 0 / 6 (0.00%)  | 0 / 13 (0.00%) | 0 / 4 (0.00%)  |
| occurrences (all)                              | 0              | 0              | 0              |
| Infusion related reaction                      |                |                |                |
| subjects affected / exposed                    | 0 / 6 (0.00%)  | 0 / 13 (0.00%) | 0 / 4 (0.00%)  |
| occurrences (all)                              | 0              | 0              | 0              |
| Limb injury                                    |                |                |                |
| subjects affected / exposed                    | 0 / 6 (0.00%)  | 0 / 13 (0.00%) | 0 / 4 (0.00%)  |
| occurrences (all)                              | 0              | 0              | 0              |
| Muscle rupture                                 |                |                |                |
| subjects affected / exposed                    | 0 / 6 (0.00%)  | 0 / 13 (0.00%) | 0 / 4 (0.00%)  |
| occurrences (all)                              | 0              | 0              | 0              |
| Overdose                                       |                |                |                |
| subjects affected / exposed                    | 1 / 6 (16.67%) | 0 / 13 (0.00%) | 1 / 4 (25.00%) |
| occurrences (all)                              | 1              | 0              | 1              |
| Post procedural haematoma                      |                |                |                |
| subjects affected / exposed                    | 0 / 6 (0.00%)  | 0 / 13 (0.00%) | 0 / 4 (0.00%)  |
| occurrences (all)                              | 0              | 0              | 0              |
| Skin abrasion                                  |                |                |                |

|                                  |               |                |               |
|----------------------------------|---------------|----------------|---------------|
| subjects affected / exposed      | 0 / 6 (0.00%) | 0 / 13 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all)                | 0             | 0              | 0             |
| Procedural pain                  |               |                |               |
| subjects affected / exposed      | 0 / 6 (0.00%) | 1 / 13 (7.69%) | 0 / 4 (0.00%) |
| occurrences (all)                | 0             | 1              | 0             |
| Subcutaneous haematoma           |               |                |               |
| subjects affected / exposed      | 0 / 6 (0.00%) | 0 / 13 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all)                | 0             | 0              | 0             |
| Skin laceration                  |               |                |               |
| subjects affected / exposed      | 0 / 6 (0.00%) | 0 / 13 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all)                | 0             | 0              | 0             |
| Tongue injury                    |               |                |               |
| subjects affected / exposed      | 0 / 6 (0.00%) | 1 / 13 (7.69%) | 0 / 4 (0.00%) |
| occurrences (all)                | 0             | 1              | 0             |
| Tooth fracture                   |               |                |               |
| subjects affected / exposed      | 0 / 6 (0.00%) | 0 / 13 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all)                | 0             | 0              | 0             |
| Urinary tract stoma complication |               |                |               |
| subjects affected / exposed      | 0 / 6 (0.00%) | 0 / 13 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all)                | 0             | 0              | 0             |
| Cardiac disorders                |               |                |               |
| Atrial fibrillation              |               |                |               |
| subjects affected / exposed      | 0 / 6 (0.00%) | 1 / 13 (7.69%) | 0 / 4 (0.00%) |
| occurrences (all)                | 0             | 1              | 0             |
| Angina pectoris                  |               |                |               |
| subjects affected / exposed      | 0 / 6 (0.00%) | 0 / 13 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all)                | 0             | 0              | 0             |
| Palpitations                     |               |                |               |
| subjects affected / exposed      | 0 / 6 (0.00%) | 1 / 13 (7.69%) | 0 / 4 (0.00%) |
| occurrences (all)                | 0             | 2              | 0             |
| Tachycardia                      |               |                |               |
| subjects affected / exposed      | 0 / 6 (0.00%) | 0 / 13 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all)                | 0             | 0              | 0             |
| Sinus tachycardia                |               |                |               |
| subjects affected / exposed      | 0 / 6 (0.00%) | 0 / 13 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all)                | 0             | 0              | 0             |

|  |                     |                      |                     |
|--|---------------------|----------------------|---------------------|
| Ventricular arrhythmia<br>subjects affected / exposed<br>occurrences (all)   | 0 / 6 (0.00%)<br>0  | 0 / 13 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0  |
| Nervous system disorders   |                     |                      |                     |
| Ageusia<br>subjects affected / exposed<br>occurrences (all)                  | 0 / 6 (0.00%)<br>0  | 0 / 13 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0  |
| Agnosia<br>subjects affected / exposed<br>occurrences (all)                  | 0 / 6 (0.00%)<br>0  | 0 / 13 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0  |
| Amnesia<br>subjects affected / exposed<br>occurrences (all)                  | 0 / 6 (0.00%)<br>0  | 0 / 13 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0  |
| Cauda equina syndrome<br>subjects affected / exposed<br>occurrences (all)    | 0 / 6 (0.00%)<br>0  | 0 / 13 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0  |
| Disturbance in attention<br>subjects affected / exposed<br>occurrences (all) | 0 / 6 (0.00%)<br>0  | 1 / 13 (7.69%)<br>1  | 0 / 4 (0.00%)<br>0  |
| Dizziness<br>subjects affected / exposed<br>occurrences (all)                | 0 / 6 (0.00%)<br>0  | 1 / 13 (7.69%)<br>1  | 0 / 4 (0.00%)<br>0  |
| Dizziness postural<br>subjects affected / exposed<br>occurrences (all)       | 0 / 6 (0.00%)<br>0  | 0 / 13 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0  |
| Headache<br>subjects affected / exposed<br>occurrences (all)                 | 1 / 6 (16.67%)<br>1 | 3 / 13 (23.08%)<br>5 | 1 / 4 (25.00%)<br>1 |
| Dysgeusia<br>subjects affected / exposed<br>occurrences (all)                | 2 / 6 (33.33%)<br>2 | 3 / 13 (23.08%)<br>3 | 2 / 4 (50.00%)<br>2 |
| Motor dysfunction<br>subjects affected / exposed<br>occurrences (all)        | 0 / 6 (0.00%)<br>0  | 0 / 13 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0  |
| Neuropathy peripheral  |                     |                      |                     |

|                                      |                |                 |               |
|--------------------------------------|----------------|-----------------|---------------|
| subjects affected / exposed          | 0 / 6 (0.00%)  | 0 / 13 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)                    | 0              | 0               | 0             |
| Peripheral sensory neuropathy        |                |                 |               |
| subjects affected / exposed          | 0 / 6 (0.00%)  | 0 / 13 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)                    | 0              | 0               | 0             |
| Paraesthesia                         |                |                 |               |
| subjects affected / exposed          | 0 / 6 (0.00%)  | 0 / 13 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)                    | 0              | 0               | 0             |
| Presyncope                           |                |                 |               |
| subjects affected / exposed          | 1 / 6 (16.67%) | 0 / 13 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)                    | 1              | 0               | 0             |
| Radiculopathy                        |                |                 |               |
| subjects affected / exposed          | 0 / 6 (0.00%)  | 0 / 13 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)                    | 0              | 0               | 0             |
| Syncope                              |                |                 |               |
| subjects affected / exposed          | 0 / 6 (0.00%)  | 0 / 13 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)                    | 0              | 0               | 0             |
| Somnolence                           |                |                 |               |
| subjects affected / exposed          | 0 / 6 (0.00%)  | 0 / 13 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)                    | 0              | 0               | 0             |
| Sciatica                             |                |                 |               |
| subjects affected / exposed          | 0 / 6 (0.00%)  | 1 / 13 (7.69%)  | 0 / 4 (0.00%) |
| occurrences (all)                    | 0              | 1               | 0             |
| Taste disorder                       |                |                 |               |
| subjects affected / exposed          | 0 / 6 (0.00%)  | 1 / 13 (7.69%)  | 0 / 4 (0.00%) |
| occurrences (all)                    | 0              | 1               | 0             |
| Blood and lymphatic system disorders |                |                 |               |
| Anaemia                              |                |                 |               |
| subjects affected / exposed          | 2 / 6 (33.33%) | 4 / 13 (30.77%) | 0 / 4 (0.00%) |
| occurrences (all)                    | 3              | 4               | 0             |
| Coagulopathy                         |                |                 |               |
| subjects affected / exposed          | 0 / 6 (0.00%)  | 0 / 13 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)                    | 0              | 0               | 0             |
| Eosinophilia                         |                |                 |               |
| subjects affected / exposed          | 0 / 6 (0.00%)  | 0 / 13 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)                    | 0              | 0               | 0             |

|  |                     |                       |                     |
|--|---------------------|-----------------------|---------------------|
| Lymph node haemorrhage<br>subjects affected / exposed<br>occurrences (all)   | 0 / 6 (0.00%)<br>0  | 0 / 13 (0.00%)<br>0   | 0 / 4 (0.00%)<br>0  |
| Lymph node pain<br>subjects affected / exposed<br>occurrences (all)          | 0 / 6 (0.00%)<br>0  | 0 / 13 (0.00%)<br>0   | 0 / 4 (0.00%)<br>0  |
| Lymphadenopathy<br>subjects affected / exposed<br>occurrences (all)          | 0 / 6 (0.00%)<br>0  | 0 / 13 (0.00%)<br>0   | 0 / 4 (0.00%)<br>0  |
| Neutropenia<br>subjects affected / exposed<br>occurrences (all)              | 0 / 6 (0.00%)<br>0  | 3 / 13 (23.08%)<br>10 | 0 / 4 (0.00%)<br>0  |
| Lymphopenia<br>subjects affected / exposed<br>occurrences (all)              | 1 / 6 (16.67%)<br>2 | 1 / 13 (7.69%)<br>1   | 0 / 4 (0.00%)<br>0  |
| Thrombocytopenia<br>subjects affected / exposed<br>occurrences (all)         | 3 / 6 (50.00%)<br>3 | 6 / 13 (46.15%)<br>10 | 2 / 4 (50.00%)<br>4 |
| Ear and labyrinth disorders  |                     |                       |                     |
| Ear congestion<br>subjects affected / exposed<br>occurrences (all)           | 0 / 6 (0.00%)<br>0  | 1 / 13 (7.69%)<br>1   | 0 / 4 (0.00%)<br>0  |
| Ear haemorrhage<br>subjects affected / exposed<br>occurrences (all)          | 0 / 6 (0.00%)<br>0  | 1 / 13 (7.69%)<br>1   | 0 / 4 (0.00%)<br>0  |
| Ear pain<br>subjects affected / exposed<br>occurrences (all)                 | 0 / 6 (0.00%)<br>0  | 0 / 13 (0.00%)<br>0   | 0 / 4 (0.00%)<br>0  |
| Vertigo<br>subjects affected / exposed<br>occurrences (all)                  | 0 / 6 (0.00%)<br>0  | 0 / 13 (0.00%)<br>0   | 0 / 4 (0.00%)<br>0  |
| Eye disorders  |                     |                       |                     |
| Conjunctival haemorrhage<br>subjects affected / exposed<br>occurrences (all) | 0 / 6 (0.00%)<br>0  | 0 / 13 (0.00%)<br>0   | 0 / 4 (0.00%)<br>0  |
| Dry eye  |                     |                       |                     |

|                             |               |                |                |
|-----------------------------|---------------|----------------|----------------|
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 13 (0.00%) | 0 / 4 (0.00%)  |
| occurrences (all)           | 0             | 0              | 0              |
| Vitreous haemorrhage        |               |                |                |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 13 (0.00%) | 0 / 4 (0.00%)  |
| occurrences (all)           | 0             | 0              | 0              |
| Vision blurred              |               |                |                |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 13 (0.00%) | 0 / 4 (0.00%)  |
| occurrences (all)           | 0             | 0              | 0              |
| Periorbital oedema          |               |                |                |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 13 (0.00%) | 0 / 4 (0.00%)  |
| occurrences (all)           | 0             | 0              | 0              |
| Gastrointestinal disorders  |               |                |                |
| Abdominal pain upper        |               |                |                |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 13 (7.69%) | 1 / 4 (25.00%) |
| occurrences (all)           | 0             | 1              | 1              |
| Abdominal pain              |               |                |                |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 13 (0.00%) | 0 / 4 (0.00%)  |
| occurrences (all)           | 0             | 0              | 0              |
| Abdominal distension        |               |                |                |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 13 (0.00%) | 0 / 4 (0.00%)  |
| occurrences (all)           | 0             | 0              | 0              |
| Anal fissure                |               |                |                |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 13 (7.69%) | 0 / 4 (0.00%)  |
| occurrences (all)           | 0             | 1              | 0              |
| Anal haemorrhage            |               |                |                |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 13 (0.00%) | 0 / 4 (0.00%)  |
| occurrences (all)           | 0             | 0              | 0              |
| Aphthous ulcer              |               |                |                |
| subjects affected / exposed | 0 / 6 (0.00%) | 1 / 13 (7.69%) | 0 / 4 (0.00%)  |
| occurrences (all)           | 0             | 1              | 0              |
| Angular cheilitis           |               |                |                |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 13 (0.00%) | 0 / 4 (0.00%)  |
| occurrences (all)           | 0             | 0              | 0              |
| Anal inflammation           |               |                |                |
| subjects affected / exposed | 0 / 6 (0.00%) | 0 / 13 (0.00%) | 0 / 4 (0.00%)  |
| occurrences (all)           | 0             | 0              | 0              |



|                                  |                |                 |                |
|----------------------------------|----------------|-----------------|----------------|
| Ascites                          |                |                 |                |
| subjects affected / exposed      | 0 / 6 (0.00%)  | 0 / 13 (0.00%)  | 1 / 4 (25.00%) |
| occurrences (all)                | 0              | 0               | 2              |
| Constipation                     |                |                 |                |
| subjects affected / exposed      | 0 / 6 (0.00%)  | 2 / 13 (15.38%) | 1 / 4 (25.00%) |
| occurrences (all)                | 0              | 2               | 1              |
| Diarrhoea                        |                |                 |                |
| subjects affected / exposed      | 2 / 6 (33.33%) | 6 / 13 (46.15%) | 3 / 4 (75.00%) |
| occurrences (all)                | 2              | 9               | 5              |
| Dry mouth                        |                |                 |                |
| subjects affected / exposed      | 0 / 6 (0.00%)  | 3 / 13 (23.08%) | 0 / 4 (0.00%)  |
| occurrences (all)                | 0              | 3               | 0              |
| Dyspepsia                        |                |                 |                |
| subjects affected / exposed      | 0 / 6 (0.00%)  | 0 / 13 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                | 0              | 0               | 0              |
| Dysphagia                        |                |                 |                |
| subjects affected / exposed      | 1 / 6 (16.67%) | 0 / 13 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                | 1              | 0               | 0              |
| Flatulence                       |                |                 |                |
| subjects affected / exposed      | 0 / 6 (0.00%)  | 0 / 13 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                | 0              | 0               | 0              |
| Gastritis                        |                |                 |                |
| subjects affected / exposed      | 0 / 6 (0.00%)  | 0 / 13 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                | 0              | 0               | 0              |
| Gastritis erosive                |                |                 |                |
| subjects affected / exposed      | 0 / 6 (0.00%)  | 0 / 13 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                | 0              | 0               | 0              |
| Gastrointestinal disorder        |                |                 |                |
| subjects affected / exposed      | 0 / 6 (0.00%)  | 0 / 13 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                | 0              | 0               | 0              |
| Gastrooesophageal reflux disease |                |                 |                |
| subjects affected / exposed      | 0 / 6 (0.00%)  | 0 / 13 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                | 0              | 0               | 0              |
| Haemorrhoids                     |                |                 |                |
| subjects affected / exposed      | 0 / 6 (0.00%)  | 1 / 13 (7.69%)  | 0 / 4 (0.00%)  |
| occurrences (all)                | 0              | 1               | 0              |

|                                    |                |                 |                |
|------------------------------------|----------------|-----------------|----------------|
| Lip dry                            |                |                 |                |
| subjects affected / exposed        | 0 / 6 (0.00%)  | 0 / 13 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                  | 0              | 0               | 0              |
| Melaena                            |                |                 |                |
| subjects affected / exposed        | 1 / 6 (16.67%) | 0 / 13 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                  | 1              | 0               | 0              |
| Lower gastrointestinal haemorrhage |                |                 |                |
| subjects affected / exposed        | 0 / 6 (0.00%)  | 1 / 13 (7.69%)  | 0 / 4 (0.00%)  |
| occurrences (all)                  | 0              | 1               | 0              |
| Nausea                             |                |                 |                |
| subjects affected / exposed        | 2 / 6 (33.33%) | 2 / 13 (15.38%) | 1 / 4 (25.00%) |
| occurrences (all)                  | 2              | 2               | 3              |
| Odynophagia                        |                |                 |                |
| subjects affected / exposed        | 0 / 6 (0.00%)  | 0 / 13 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                  | 0              | 0               | 0              |
| Oral mucosal erythema              |                |                 |                |
| subjects affected / exposed        | 1 / 6 (16.67%) | 0 / 13 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                  | 1              | 0               | 0              |
| Retching                           |                |                 |                |
| subjects affected / exposed        | 0 / 6 (0.00%)  | 0 / 13 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                  | 0              | 0               | 0              |
| Stomatitis                         |                |                 |                |
| subjects affected / exposed        | 1 / 6 (16.67%) | 0 / 13 (0.00%)  | 1 / 4 (25.00%) |
| occurrences (all)                  | 1              | 0               | 1              |
| Subileus                           |                |                 |                |
| subjects affected / exposed        | 0 / 6 (0.00%)  | 0 / 13 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                  | 0              | 0               | 0              |
| Toothache                          |                |                 |                |
| subjects affected / exposed        | 0 / 6 (0.00%)  | 0 / 13 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                  | 0              | 0               | 0              |
| Vomiting                           |                |                 |                |
| subjects affected / exposed        | 2 / 6 (33.33%) | 1 / 13 (7.69%)  | 1 / 4 (25.00%) |
| occurrences (all)                  | 5              | 1               | 2              |
| Hepatobiliary disorders            |                |                 |                |
| Cholangitis                        |                |                 |                |

|  |                |                 |                |
|--|----------------|-----------------|----------------|
| subjects affected / exposed            | 0 / 6 (0.00%)  | 1 / 13 (7.69%)  | 0 / 4 (0.00%)  |
| occurrences (all)                      | 0              | 1               | 0              |
| Hepatic cytolysis                      |                |                 |                |
| subjects affected / exposed            | 0 / 6 (0.00%)  | 1 / 13 (7.69%)  | 0 / 4 (0.00%)  |
| occurrences (all)                      | 0              | 1               | 0              |
| Hepatic pain                           |                |                 |                |
| subjects affected / exposed            | 0 / 6 (0.00%)  | 0 / 13 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                      | 0              | 0               | 0              |
| Skin and subcutaneous tissue disorders |                |                 |                |
| Dermatitis psoriasiform                |                |                 |                |
| subjects affected / exposed            | 0 / 6 (0.00%)  | 1 / 13 (7.69%)  | 0 / 4 (0.00%)  |
| occurrences (all)                      | 0              | 1               | 0              |
| Dermatitis acneiform                   |                |                 |                |
| subjects affected / exposed            | 1 / 6 (16.67%) | 2 / 13 (15.38%) | 1 / 4 (25.00%) |
| occurrences (all)                      | 1              | 3               | 1              |
| Dry skin                               |                |                 |                |
| subjects affected / exposed            | 1 / 6 (16.67%) | 1 / 13 (7.69%)  | 0 / 4 (0.00%)  |
| occurrences (all)                      | 3              | 1               | 0              |
| Intertrigo                             |                |                 |                |
| subjects affected / exposed            | 0 / 6 (0.00%)  | 0 / 13 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                      | 0              | 0               | 0              |
| Macule                                 |                |                 |                |
| subjects affected / exposed            | 1 / 6 (16.67%) | 0 / 13 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                      | 1              | 0               | 0              |
| Night sweats                           |                |                 |                |
| subjects affected / exposed            | 0 / 6 (0.00%)  | 0 / 13 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                      | 0              | 0               | 0              |
| Eczema                                 |                |                 |                |
| subjects affected / exposed            | 0 / 6 (0.00%)  | 1 / 13 (7.69%)  | 0 / 4 (0.00%)  |
| occurrences (all)                      | 0              | 2               | 0              |
| Erythema                               |                |                 |                |
| subjects affected / exposed            | 0 / 6 (0.00%)  | 1 / 13 (7.69%)  | 0 / 4 (0.00%)  |
| occurrences (all)                      | 0              | 2               | 0              |
| Prurigo                                |                |                 |                |
| subjects affected / exposed            | 0 / 6 (0.00%)  | 0 / 13 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                      | 0              | 0               | 0              |

|                             |                |                 |                |
|-----------------------------|----------------|-----------------|----------------|
| Pruritus                    |                |                 |                |
| subjects affected / exposed | 1 / 6 (16.67%) | 1 / 13 (7.69%)  | 0 / 4 (0.00%)  |
| occurrences (all)           | 1              | 1               | 0              |
| Psoriasis                   |                |                 |                |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 13 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)           | 1              | 0               | 0              |
| Petechiae                   |                |                 |                |
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 13 (0.00%)  | 1 / 4 (25.00%) |
| occurrences (all)           | 0              | 0               | 1              |
| Skin ulcer                  |                |                 |                |
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 13 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)           | 0              | 0               | 0              |
| Rash                        |                |                 |                |
| subjects affected / exposed | 0 / 6 (0.00%)  | 3 / 13 (23.08%) | 0 / 4 (0.00%)  |
| occurrences (all)           | 0              | 3               | 0              |
| Rash maculo-papular         |                |                 |                |
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 13 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)           | 0              | 0               | 0              |
| Purpura                     |                |                 |                |
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 13 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)           | 0              | 0               | 0              |
| Urticaria                   |                |                 |                |
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 13 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)           | 0              | 0               | 0              |
| Renal and urinary disorders |                |                 |                |
| Dysuria                     |                |                 |                |
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 13 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)           | 0              | 0               | 0              |
| Haematuria                  |                |                 |                |
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 13 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)           | 0              | 0               | 0              |
| Pollakiuria                 |                |                 |                |
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 13 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)           | 0              | 0               | 0              |
| Urinary tract pain          |                |                 |                |

|   |                |                 |               |
|---|----------------|-----------------|---------------|
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 13 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)                               | 0              | 0               | 0             |
| Urinary retention                               |                |                 |               |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 13 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)                               | 0              | 0               | 0             |
| Renal failure                                   |                |                 |               |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 13 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)                               | 0              | 0               | 0             |
| Endocrine disorders                             |                |                 |               |
| Hyperthyroidism                                 |                |                 |               |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 13 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)                               | 0              | 0               | 0             |
| Musculoskeletal and connective tissue disorders |                |                 |               |
| Arthralgia                                      |                |                 |               |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 13 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)                               | 0              | 0               | 0             |
| Back pain                                       |                |                 |               |
| subjects affected / exposed                     | 1 / 6 (16.67%) | 2 / 13 (15.38%) | 0 / 4 (0.00%) |
| occurrences (all)                               | 1              | 2               | 0             |
| Bone pain                                       |                |                 |               |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 13 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)                               | 0              | 0               | 0             |
| Flank pain                                      |                |                 |               |
| subjects affected / exposed                     | 1 / 6 (16.67%) | 0 / 13 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)                               | 1              | 0               | 0             |
| Groin pain                                      |                |                 |               |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 0 / 13 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)                               | 0              | 0               | 0             |
| Muscular weakness                               |                |                 |               |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 2 / 13 (15.38%) | 0 / 4 (0.00%) |
| occurrences (all)                               | 0              | 2               | 0             |
| Muscle spasms                                   |                |                 |               |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 1 / 13 (7.69%)  | 0 / 4 (0.00%) |
| occurrences (all)                               | 0              | 1               | 0             |
| Myalgia   |                |                 |               |

|                               |               |                 |               |
|-------------------------------|---------------|-----------------|---------------|
| subjects affected / exposed   | 0 / 6 (0.00%) | 0 / 13 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)             | 0             | 0               | 0             |
| Neck pain                     |               |                 |               |
| subjects affected / exposed   | 0 / 6 (0.00%) | 0 / 13 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)             | 0             | 0               | 0             |
| Pain in extremity             |               |                 |               |
| subjects affected / exposed   | 0 / 6 (0.00%) | 2 / 13 (15.38%) | 0 / 4 (0.00%) |
| occurrences (all)             | 0             | 3               | 0             |
| Pubic pain                    |               |                 |               |
| subjects affected / exposed   | 0 / 6 (0.00%) | 0 / 13 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)             | 0             | 0               | 0             |
| Infections and infestations   |               |                 |               |
| Bronchitis                    |               |                 |               |
| subjects affected / exposed   | 0 / 6 (0.00%) | 2 / 13 (15.38%) | 0 / 4 (0.00%) |
| occurrences (all)             | 0             | 2               | 0             |
| Bronchitis viral              |               |                 |               |
| subjects affected / exposed   | 0 / 6 (0.00%) | 0 / 13 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)             | 0             | 0               | 0             |
| Clostridial infection         |               |                 |               |
| subjects affected / exposed   | 0 / 6 (0.00%) | 1 / 13 (7.69%)  | 0 / 4 (0.00%) |
| occurrences (all)             | 0             | 2               | 0             |
| Clostridium difficile colitis |               |                 |               |
| subjects affected / exposed   | 0 / 6 (0.00%) | 0 / 13 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)             | 0             | 0               | 0             |
| Conjunctivitis                |               |                 |               |
| subjects affected / exposed   | 0 / 6 (0.00%) | 0 / 13 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)             | 0             | 0               | 0             |
| Erysipelas                    |               |                 |               |
| subjects affected / exposed   | 0 / 6 (0.00%) | 0 / 13 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)             | 0             | 0               | 0             |
| Diverticulitis                |               |                 |               |
| subjects affected / exposed   | 0 / 6 (0.00%) | 0 / 13 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)             | 0             | 0               | 0             |
| Cystitis                      |               |                 |               |
| subjects affected / exposed   | 0 / 6 (0.00%) | 0 / 13 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)             | 0             | 0               | 0             |

|                                     |                |                |                |
|-------------------------------------|----------------|----------------|----------------|
| Gastroenteritis                     |                |                |                |
| subjects affected / exposed         | 0 / 6 (0.00%)  | 0 / 13 (0.00%) | 1 / 4 (25.00%) |
| occurrences (all)                   | 0              | 0              | 1              |
| Folliculitis                        |                |                |                |
| subjects affected / exposed         | 1 / 6 (16.67%) | 0 / 13 (0.00%) | 0 / 4 (0.00%)  |
| occurrences (all)                   | 1              | 0              | 0              |
| Escherichia urinary tract infection |                |                |                |
| subjects affected / exposed         | 0 / 6 (0.00%)  | 0 / 13 (0.00%) | 0 / 4 (0.00%)  |
| occurrences (all)                   | 0              | 0              | 0              |
| Genital herpes simplex              |                |                |                |
| subjects affected / exposed         | 1 / 6 (16.67%) | 0 / 13 (0.00%) | 0 / 4 (0.00%)  |
| occurrences (all)                   | 1              | 0              | 0              |
| Genital infection fungal            |                |                |                |
| subjects affected / exposed         | 0 / 6 (0.00%)  | 0 / 13 (0.00%) | 0 / 4 (0.00%)  |
| occurrences (all)                   | 0              | 0              | 0              |
| Herpes dermatitis                   |                |                |                |
| subjects affected / exposed         | 0 / 6 (0.00%)  | 0 / 13 (0.00%) | 1 / 4 (25.00%) |
| occurrences (all)                   | 0              | 0              | 1              |
| Impetigo                            |                |                |                |
| subjects affected / exposed         | 0 / 6 (0.00%)  | 0 / 13 (0.00%) | 0 / 4 (0.00%)  |
| occurrences (all)                   | 0              | 0              | 0              |
| Herpes zoster                       |                |                |                |
| subjects affected / exposed         | 0 / 6 (0.00%)  | 0 / 13 (0.00%) | 0 / 4 (0.00%)  |
| occurrences (all)                   | 0              | 0              | 0              |
| Influenza                           |                |                |                |
| subjects affected / exposed         | 1 / 6 (16.67%) | 0 / 13 (0.00%) | 0 / 4 (0.00%)  |
| occurrences (all)                   | 1              | 0              | 0              |
| Infection                           |                |                |                |
| subjects affected / exposed         | 0 / 6 (0.00%)  | 0 / 13 (0.00%) | 0 / 4 (0.00%)  |
| occurrences (all)                   | 0              | 0              | 0              |
| Nasopharyngitis                     |                |                |                |
| subjects affected / exposed         | 1 / 6 (16.67%) | 0 / 13 (0.00%) | 0 / 4 (0.00%)  |
| occurrences (all)                   | 1              | 0              | 0              |
| Oesophageal infection               |                |                |                |
| subjects affected / exposed         | 1 / 6 (16.67%) | 0 / 13 (0.00%) | 0 / 4 (0.00%)  |
| occurrences (all)                   | 1              | 0              | 0              |

|                                       |                |                |               |
|---------------------------------------|----------------|----------------|---------------|
| Pharyngitis                           |                |                |               |
| subjects affected / exposed           | 0 / 6 (0.00%)  | 1 / 13 (7.69%) | 0 / 4 (0.00%) |
| occurrences (all)                     | 0              | 1              | 0             |
| Oral herpes                           |                |                |               |
| subjects affected / exposed           | 1 / 6 (16.67%) | 0 / 13 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all)                     | 1              | 0              | 0             |
| Pneumonia                             |                |                |               |
| subjects affected / exposed           | 0 / 6 (0.00%)  | 0 / 13 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all)                     | 0              | 0              | 0             |
| Rash pustular                         |                |                |               |
| subjects affected / exposed           | 0 / 6 (0.00%)  | 0 / 13 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all)                     | 0              | 0              | 0             |
| Respiratory tract infection           |                |                |               |
| subjects affected / exposed           | 0 / 6 (0.00%)  | 1 / 13 (7.69%) | 0 / 4 (0.00%) |
| occurrences (all)                     | 0              | 1              | 0             |
| Respiratory tract infection bacterial |                |                |               |
| subjects affected / exposed           | 1 / 6 (16.67%) | 0 / 13 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all)                     | 1              | 0              | 0             |
| Sinusitis                             |                |                |               |
| subjects affected / exposed           | 0 / 6 (0.00%)  | 0 / 13 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all)                     | 0              | 0              | 0             |
| Tooth abscess                         |                |                |               |
| subjects affected / exposed           | 0 / 6 (0.00%)  | 0 / 13 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all)                     | 0              | 0              | 0             |
| Tooth infection                       |                |                |               |
| subjects affected / exposed           | 0 / 6 (0.00%)  | 0 / 13 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all)                     | 0              | 0              | 0             |
| Tracheitis                            |                |                |               |
| subjects affected / exposed           | 0 / 6 (0.00%)  | 1 / 13 (7.69%) | 0 / 4 (0.00%) |
| occurrences (all)                     | 0              | 1              | 0             |
| Upper respiratory tract infection     |                |                |               |
| subjects affected / exposed           | 0 / 6 (0.00%)  | 0 / 13 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all)                     | 0              | 0              | 0             |
| Urinary tract infection enterococcal  |                |                |               |
| subjects affected / exposed           | 0 / 6 (0.00%)  | 0 / 13 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all)                     | 0              | 0              | 0             |



|                                    |                |                 |                |
|------------------------------------|----------------|-----------------|----------------|
| Urinary tract infection            |                |                 |                |
| subjects affected / exposed        | 0 / 6 (0.00%)  | 1 / 13 (7.69%)  | 0 / 4 (0.00%)  |
| occurrences (all)                  | 0              | 1               | 0              |
| Mucosal infection                  |                |                 |                |
| subjects affected / exposed        | 0 / 6 (0.00%)  | 0 / 13 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                  | 0              | 0               | 0              |
| Stoma site infection               |                |                 |                |
| subjects affected / exposed        | 0 / 6 (0.00%)  | 0 / 13 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                  | 0              | 0               | 0              |
| Metabolism and nutrition disorders |                |                 |                |
| Acidosis                           |                |                 |                |
| subjects affected / exposed        | 0 / 6 (0.00%)  | 0 / 13 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                  | 0              | 0               | 0              |
| Decreased appetite                 |                |                 |                |
| subjects affected / exposed        | 1 / 6 (16.67%) | 4 / 13 (30.77%) | 1 / 4 (25.00%) |
| occurrences (all)                  | 2              | 4               | 2              |
| Cell death                         |                |                 |                |
| subjects affected / exposed        | 0 / 6 (0.00%)  | 0 / 13 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                  | 0              | 0               | 0              |
| Dehydration                        |                |                 |                |
| subjects affected / exposed        | 0 / 6 (0.00%)  | 1 / 13 (7.69%)  | 0 / 4 (0.00%)  |
| occurrences (all)                  | 0              | 1               | 0              |
| Fluid retention                    |                |                 |                |
| subjects affected / exposed        | 0 / 6 (0.00%)  | 0 / 13 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                  | 0              | 0               | 0              |
| Folate deficiency                  |                |                 |                |
| subjects affected / exposed        | 0 / 6 (0.00%)  | 1 / 13 (7.69%)  | 0 / 4 (0.00%)  |
| occurrences (all)                  | 0              | 1               | 0              |
| Gout                               |                |                 |                |
| subjects affected / exposed        | 0 / 6 (0.00%)  | 0 / 13 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                  | 0              | 0               | 0              |
| Hypercalcaemia                     |                |                 |                |
| subjects affected / exposed        | 0 / 6 (0.00%)  | 0 / 13 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                  | 0              | 0               | 0              |
| Hyperkalaemia                      |                |                 |                |

|                             |                |                |                |
|-----------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 13 (0.00%) | 0 / 4 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0              |
| Hyperglycaemia              |                |                |                |
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 13 (0.00%) | 1 / 4 (25.00%) |
| occurrences (all)           | 0              | 0              | 2              |
| Hyperphosphataemia          |                |                |                |
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 13 (0.00%) | 0 / 4 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0              |
| Hypoalbuminaemia            |                |                |                |
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 13 (0.00%) | 0 / 4 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0              |
| Hypocalcaemia               |                |                |                |
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 13 (0.00%) | 0 / 4 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0              |
| Hypokalaemia                |                |                |                |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 13 (0.00%) | 0 / 4 (0.00%)  |
| occurrences (all)           | 1              | 0              | 0              |
| Hypomagnesaemia             |                |                |                |
| subjects affected / exposed | 1 / 6 (16.67%) | 0 / 13 (0.00%) | 0 / 4 (0.00%)  |
| occurrences (all)           | 1              | 0              | 0              |
| Hyponatraemia               |                |                |                |
| subjects affected / exposed | 0 / 6 (0.00%)  | 0 / 13 (0.00%) | 0 / 4 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0              |
| Hypophosphataemia           |                |                |                |
| subjects affected / exposed | 3 / 6 (50.00%) | 1 / 13 (7.69%) | 0 / 4 (0.00%)  |
| occurrences (all)           | 5              | 1              | 0              |
| Malnutrition                |                |                |                |
| subjects affected / exposed | 0 / 6 (0.00%)  | 1 / 13 (7.69%) | 0 / 4 (0.00%)  |
| occurrences (all)           | 0              | 1              | 0              |

| <b>Non-serious adverse events</b>                                   | Phase Ia - Schedule A: 0.5 mg BI 89499 | Phase Ia - Schedule A: 5 mg BI 894999 | Phase Ia - Schedule C: 7/3.5 mg BI 894999 |
|---|--|---------------------------------------|---|
| Total subjects affected by non-serious adverse events               |  |                                       |   |
| subjects affected / exposed   | 2 / 2 (100.00%)                        | 2 / 2 (100.00%)                       | 12 / 12 (100.00%)                         |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |  |                                       |   |

|   |                     |                      |                        |
|---|---------------------|----------------------|------------------------|
| Tumour pain<br>subjects affected / exposed<br>occurrences (all)             | 0 / 2 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0   | 0 / 12 (0.00%)<br>0    |
| Vascular disorders  |                     |                      |                        |
| Hypotension<br>subjects affected / exposed<br>occurrences (all)             | 0 / 2 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0   | 0 / 12 (0.00%)<br>0    |
| Hypertension<br>subjects affected / exposed<br>occurrences (all)            | 1 / 2 (50.00%)<br>1 | 0 / 2 (0.00%)<br>0   | 3 / 12 (25.00%)<br>3   |
| Haematoma<br>subjects affected / exposed<br>occurrences (all)               | 0 / 2 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0   | 0 / 12 (0.00%)<br>0    |
| Orthostatic hypotension<br>subjects affected / exposed<br>occurrences (all) | 0 / 2 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0   | 1 / 12 (8.33%)<br>1    |
| Pallor<br>subjects affected / exposed<br>occurrences (all)                  | 0 / 2 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0   | 0 / 12 (0.00%)<br>0    |
| General disorders and administration<br>site conditions                     |                     |                      |                        |
| Chest discomfort<br>subjects affected / exposed<br>occurrences (all)        | 0 / 2 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0   | 0 / 12 (0.00%)<br>0    |
| Asthenia<br>subjects affected / exposed<br>occurrences (all)                | 0 / 2 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0   | 0 / 12 (0.00%)<br>0    |
| Chest pain<br>subjects affected / exposed<br>occurrences (all)              | 0 / 2 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0   | 0 / 12 (0.00%)<br>0    |
| Fatigue<br>subjects affected / exposed<br>occurrences (all)                 | 1 / 2 (50.00%)<br>1 | 2 / 2 (100.00%)<br>4 | 10 / 12 (83.33%)<br>11 |
| Facial pain<br>subjects affected / exposed<br>occurrences (all)             | 1 / 2 (50.00%)<br>2 | 0 / 2 (0.00%)<br>0   | 0 / 12 (0.00%)<br>0    |
| Chills  |                     |                      |                        |

|                                       |                |                |                 |
|---------------------------------------|----------------|----------------|-----------------|
| subjects affected / exposed           | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 0 / 12 (0.00%)  |
| occurrences (all)                     | 0              | 0              | 0               |
| Gait disturbance                      |                |                |                 |
| subjects affected / exposed           | 1 / 2 (50.00%) | 0 / 2 (0.00%)  | 0 / 12 (0.00%)  |
| occurrences (all)                     | 1              | 0              | 0               |
| General physical health deterioration |                |                |                 |
| subjects affected / exposed           | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 0 / 12 (0.00%)  |
| occurrences (all)                     | 0              | 0              | 0               |
| Generalised oedema                    |                |                |                 |
| subjects affected / exposed           | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 0 / 12 (0.00%)  |
| occurrences (all)                     | 0              | 0              | 0               |
| Malaise                               |                |                |                 |
| subjects affected / exposed           | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 0 / 12 (0.00%)  |
| occurrences (all)                     | 0              | 0              | 0               |
| Hypothermia                           |                |                |                 |
| subjects affected / exposed           | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 1 / 12 (8.33%)  |
| occurrences (all)                     | 0              | 0              | 1               |
| Oedema peripheral                     |                |                |                 |
| subjects affected / exposed           | 1 / 2 (50.00%) | 0 / 2 (0.00%)  | 1 / 12 (8.33%)  |
| occurrences (all)                     | 2              | 0              | 1               |
| Non-cardiac chest pain                |                |                |                 |
| subjects affected / exposed           | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 0 / 12 (0.00%)  |
| occurrences (all)                     | 0              | 0              | 0               |
| Pain                                  |                |                |                 |
| subjects affected / exposed           | 0 / 2 (0.00%)  | 1 / 2 (50.00%) | 2 / 12 (16.67%) |
| occurrences (all)                     | 0              | 1              | 2               |
| Pyrexia                               |                |                |                 |
| subjects affected / exposed           | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 0 / 12 (0.00%)  |
| occurrences (all)                     | 0              | 0              | 0               |
| Peripheral swelling                   |                |                |                 |
| subjects affected / exposed           | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 0 / 12 (0.00%)  |
| occurrences (all)                     | 0              | 0              | 0               |
| Immune system disorders               |                |                |                 |
| Hypersensitivity                      |                |                |                 |
| subjects affected / exposed           | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 0 / 12 (0.00%)  |
| occurrences (all)                     | 0              | 0              | 0               |

|  |                     |                    |                      |
|--|---------------------|--------------------|----------------------|
| Iodine allergy<br>subjects affected / exposed<br>occurrences (all)           | 0 / 2 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0 | 0 / 12 (0.00%)<br>0  |
| Reproductive system and breast disorders                                     |                     |                    |                      |
| Erectile dysfunction<br>subjects affected / exposed<br>occurrences (all)     | 0 / 2 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0 | 0 / 12 (0.00%)<br>0  |
| Heavy menstrual bleeding<br>subjects affected / exposed<br>occurrences (all) | 0 / 2 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0 | 1 / 12 (8.33%)<br>1  |
| Oedema genital<br>subjects affected / exposed<br>occurrences (all)           | 0 / 2 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0 | 1 / 12 (8.33%)<br>1  |
| Perineal pain<br>subjects affected / exposed<br>occurrences (all)            | 1 / 2 (50.00%)<br>1 | 0 / 2 (0.00%)<br>0 | 0 / 12 (0.00%)<br>0  |
| Scrotal oedema<br>subjects affected / exposed<br>occurrences (all)           | 1 / 2 (50.00%)<br>1 | 0 / 2 (0.00%)<br>0 | 0 / 12 (0.00%)<br>0  |
| Testicular pain<br>subjects affected / exposed<br>occurrences (all)          | 1 / 2 (50.00%)<br>1 | 0 / 2 (0.00%)<br>0 | 0 / 12 (0.00%)<br>0  |
| Vulvovaginal discomfort<br>subjects affected / exposed<br>occurrences (all)  | 0 / 2 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0 | 0 / 12 (0.00%)<br>0  |
| Vaginal haemorrhage<br>subjects affected / exposed<br>occurrences (all)      | 0 / 2 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0 | 2 / 12 (16.67%)<br>2 |
| Respiratory, thoracic and mediastinal disorders                              |                     |                    |                      |
| Atelectasis<br>subjects affected / exposed<br>occurrences (all)              | 0 / 2 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0 | 0 / 12 (0.00%)<br>0  |
| Dysphonia<br>subjects affected / exposed<br>occurrences (all)                | 0 / 2 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0 | 0 / 12 (0.00%)<br>0  |
| Cough  |                     |                    |                      |

|                             |                |               |                 |
|-----------------------------|----------------|---------------|-----------------|
| subjects affected / exposed | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 1 / 12 (8.33%)  |
| occurrences (all)           | 0              | 0             | 1               |
| Dyspnoea                    |                |               |                 |
| subjects affected / exposed | 1 / 2 (50.00%) | 0 / 2 (0.00%) | 3 / 12 (25.00%) |
| occurrences (all)           | 1              | 0             | 5               |
| Dyspnoea exertional         |                |               |                 |
| subjects affected / exposed | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 12 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0               |
| Epistaxis                   |                |               |                 |
| subjects affected / exposed | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 2 / 12 (16.67%) |
| occurrences (all)           | 0              | 0             | 2               |
| Laryngeal inflammation      |                |               |                 |
| subjects affected / exposed | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 12 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0               |
| Haemoptysis                 |                |               |                 |
| subjects affected / exposed | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 12 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0               |
| Nasal discomfort            |                |               |                 |
| subjects affected / exposed | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 12 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0               |
| Oropharyngeal pain          |                |               |                 |
| subjects affected / exposed | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 12 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0               |
| Pharyngeal inflammation     |                |               |                 |
| subjects affected / exposed | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 12 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0               |
| Pleural effusion            |                |               |                 |
| subjects affected / exposed | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 12 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0               |
| Pleuritic pain              |                |               |                 |
| subjects affected / exposed | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 12 (0.00%)  |
| occurrences (all)           | 0              | 0             | 0               |
| Productive cough            |                |               |                 |
| subjects affected / exposed | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 1 / 12 (8.33%)  |
| occurrences (all)           | 0              | 0             | 2               |
| Rhinorrhoea                 |                |               |                 |

|                              |               |               |                 |
|------------------------------|---------------|---------------|-----------------|
| subjects affected / exposed  | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 12 (0.00%)  |
| occurrences (all)            | 0             | 0             | 0               |
| Respiratory tract congestion |               |               |                 |
| subjects affected / exposed  | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 12 (0.00%)  |
| occurrences (all)            | 0             | 0             | 0               |
| Wheezing                     |               |               |                 |
| subjects affected / exposed  | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 1 / 12 (8.33%)  |
| occurrences (all)            | 0             | 0             | 1               |
| Psychiatric disorders        |               |               |                 |
| Affective disorder           |               |               |                 |
| subjects affected / exposed  | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 12 (0.00%)  |
| occurrences (all)            | 0             | 0             | 0               |
| Agitation                    |               |               |                 |
| subjects affected / exposed  | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 12 (0.00%)  |
| occurrences (all)            | 0             | 0             | 0               |
| Anxiety                      |               |               |                 |
| subjects affected / exposed  | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 12 (0.00%)  |
| occurrences (all)            | 0             | 0             | 0               |
| Confusional state            |               |               |                 |
| subjects affected / exposed  | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 12 (0.00%)  |
| occurrences (all)            | 0             | 0             | 0               |
| Depression                   |               |               |                 |
| subjects affected / exposed  | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 12 (0.00%)  |
| occurrences (all)            | 0             | 0             | 0               |
| Insomnia                     |               |               |                 |
| subjects affected / exposed  | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 2 / 12 (16.67%) |
| occurrences (all)            | 0             | 0             | 2               |
| Hallucination                |               |               |                 |
| subjects affected / exposed  | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 12 (0.00%)  |
| occurrences (all)            | 0             | 0             | 0               |
| Personality change           |               |               |                 |
| subjects affected / exposed  | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 12 (0.00%)  |
| occurrences (all)            | 0             | 0             | 0               |
| Sleep disorder               |               |               |                 |
| subjects affected / exposed  | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 1 / 12 (8.33%)  |
| occurrences (all)            | 0             | 0             | 1               |

|   |                |                |                |
|---|----------------|----------------|----------------|
| Investigations                                  |                |                |                |
| Activated partial thromboplastin time prolonged |                |                |                |
| subjects affected / exposed                     | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 0 / 12 (0.00%) |
| occurrences (all)                               | 0              | 0              | 0              |
| Activated partial thromboplastin time shortened |                |                |                |
| subjects affected / exposed                     | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 1 / 12 (8.33%) |
| occurrences (all)                               | 0              | 0              | 1              |
| Alanine aminotransferase increased              |                |                |                |
| subjects affected / exposed                     | 0 / 2 (0.00%)  | 1 / 2 (50.00%) | 0 / 12 (0.00%) |
| occurrences (all)                               | 0              | 1              | 0              |
| Aspartate aminotransferase increased            |                |                |                |
| subjects affected / exposed                     | 0 / 2 (0.00%)  | 1 / 2 (50.00%) | 0 / 12 (0.00%) |
| occurrences (all)                               | 0              | 1              | 0              |
| Blood alkaline phosphatase increased            |                |                |                |
| subjects affected / exposed                     | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 1 / 12 (8.33%) |
| occurrences (all)                               | 0              | 0              | 1              |
| Blood antidiuretic hormone decreased            |                |                |                |
| subjects affected / exposed                     | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 0 / 12 (0.00%) |
| occurrences (all)                               | 0              | 0              | 0              |
| Blood bilirubin increased                       |                |                |                |
| subjects affected / exposed                     | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 0 / 12 (0.00%) |
| occurrences (all)                               | 0              | 0              | 0              |
| Blood creatine phosphokinase increased          |                |                |                |
| subjects affected / exposed                     | 1 / 2 (50.00%) | 1 / 2 (50.00%) | 0 / 12 (0.00%) |
| occurrences (all)                               | 1              | 1              | 0              |
| Blood creatinine increased                      |                |                |                |
| subjects affected / exposed                     | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 0 / 12 (0.00%) |
| occurrences (all)                               | 0              | 0              | 0              |
| Blood magnesium decreased                       |                |                |                |
| subjects affected / exposed                     | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 0 / 12 (0.00%) |
| occurrences (all)                               | 0              | 0              | 0              |
| Blood glucose increased                         |                |                |                |
| subjects affected / exposed                     | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 0 / 12 (0.00%) |
| occurrences (all)                               | 0              | 0              | 0              |



|   |                    |                     |                      |
|---|--------------------|---------------------|----------------------|
| C-reactive protein increased<br>subjects affected / exposed<br>occurrences (all)                | 0 / 2 (0.00%)<br>0 | 0 / 2 (0.00%)<br>0  | 0 / 12 (0.00%)<br>0  |
| Cardiac murmur<br>subjects affected / exposed<br>occurrences (all)                              | 0 / 2 (0.00%)<br>0 | 0 / 2 (0.00%)<br>0  | 0 / 12 (0.00%)<br>0  |
| Cortisol increased<br>subjects affected / exposed<br>occurrences (all)                          | 0 / 2 (0.00%)<br>0 | 0 / 2 (0.00%)<br>0  | 1 / 12 (8.33%)<br>1  |
| Echocardiogram abnormal<br>subjects affected / exposed<br>occurrences (all)                     | 0 / 2 (0.00%)<br>0 | 0 / 2 (0.00%)<br>0  | 0 / 12 (0.00%)<br>0  |
| Electrocardiogram PR prolongation<br>subjects affected / exposed<br>occurrences (all)           | 0 / 2 (0.00%)<br>0 | 0 / 2 (0.00%)<br>0  | 0 / 12 (0.00%)<br>0  |
| Ejection fraction decreased<br>subjects affected / exposed<br>occurrences (all)                 | 0 / 2 (0.00%)<br>0 | 0 / 2 (0.00%)<br>0  | 0 / 12 (0.00%)<br>0  |
| Electrocardiogram ST segment<br>elevation<br>subjects affected / exposed<br>occurrences (all)   | 0 / 2 (0.00%)<br>0 | 0 / 2 (0.00%)<br>0  | 0 / 12 (0.00%)<br>0  |
| Gamma-glutamyltransferase<br>increased<br>subjects affected / exposed<br>occurrences (all)      | 0 / 2 (0.00%)<br>0 | 0 / 2 (0.00%)<br>0  | 2 / 12 (16.67%)<br>3 |
| Electrocardiogram T wave inversion<br>subjects affected / exposed<br>occurrences (all)          | 0 / 2 (0.00%)<br>0 | 0 / 2 (0.00%)<br>0  | 0 / 12 (0.00%)<br>0  |
| International normalised ratio<br>increased<br>subjects affected / exposed<br>occurrences (all) | 0 / 2 (0.00%)<br>0 | 0 / 2 (0.00%)<br>0  | 0 / 12 (0.00%)<br>0  |
| Lymphocyte count decreased<br>subjects affected / exposed<br>occurrences (all)                  | 0 / 2 (0.00%)<br>0 | 1 / 2 (50.00%)<br>1 | 3 / 12 (25.00%)<br>3 |
| Neutrophil count decreased  |                    |                     |                      |

|  |                |               |                 |
|--|----------------|---------------|-----------------|
| subjects affected / exposed                    | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 12 (0.00%)  |
| occurrences (all)                              | 0              | 0             | 0               |
| Platelet count decreased                       |                |               |                 |
| subjects affected / exposed                    | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 2 / 12 (16.67%) |
| occurrences (all)                              | 0              | 0             | 2               |
| Prothrombin level decreased                    |                |               |                 |
| subjects affected / exposed                    | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 12 (0.00%)  |
| occurrences (all)                              | 0              | 0             | 0               |
| Troponin I increased                           |                |               |                 |
| subjects affected / exposed                    | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 12 (0.00%)  |
| occurrences (all)                              | 0              | 0             | 0               |
| Troponin T increased                           |                |               |                 |
| subjects affected / exposed                    | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 2 / 12 (16.67%) |
| occurrences (all)                              | 0              | 0             | 3               |
| Troponin increased                             |                |               |                 |
| subjects affected / exposed                    | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 12 (0.00%)  |
| occurrences (all)                              | 0              | 0             | 0               |
| Urine output decreased                         |                |               |                 |
| subjects affected / exposed                    | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 12 (0.00%)  |
| occurrences (all)                              | 0              | 0             | 0               |
| Weight decreased                               |                |               |                 |
| subjects affected / exposed                    | 1 / 2 (50.00%) | 0 / 2 (0.00%) | 2 / 12 (16.67%) |
| occurrences (all)                              | 1              | 0             | 2               |
| White blood cell count decreased               |                |               |                 |
| subjects affected / exposed                    | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 12 (0.00%)  |
| occurrences (all)                              | 0              | 0             | 0               |
| Injury, poisoning and procedural complications |                |               |                 |
| Contusion                                      |                |               |                 |
| subjects affected / exposed                    | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 12 (0.00%)  |
| occurrences (all)                              | 0              | 0             | 0               |
| Face injury                                    |                |               |                 |
| subjects affected / exposed                    | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 1 / 12 (8.33%)  |
| occurrences (all)                              | 0              | 0             | 1               |
| Infusion related reaction                      |                |               |                 |

|                                  |               |               |                |
|----------------------------------|---------------|---------------|----------------|
| subjects affected / exposed      | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                | 0             | 0             | 0              |
| Limb injury                      |               |               |                |
| subjects affected / exposed      | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 1 / 12 (8.33%) |
| occurrences (all)                | 0             | 0             | 1              |
| Muscle rupture                   |               |               |                |
| subjects affected / exposed      | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                | 0             | 0             | 0              |
| Overdose                         |               |               |                |
| subjects affected / exposed      | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                | 0             | 0             | 0              |
| Post procedural haematoma        |               |               |                |
| subjects affected / exposed      | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                | 0             | 0             | 0              |
| Skin abrasion                    |               |               |                |
| subjects affected / exposed      | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                | 0             | 0             | 0              |
| Procedural pain                  |               |               |                |
| subjects affected / exposed      | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                | 0             | 0             | 0              |
| Subcutaneous haematoma           |               |               |                |
| subjects affected / exposed      | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                | 0             | 0             | 0              |
| Skin laceration                  |               |               |                |
| subjects affected / exposed      | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                | 0             | 0             | 0              |
| Tongue injury                    |               |               |                |
| subjects affected / exposed      | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                | 0             | 0             | 0              |
| Tooth fracture                   |               |               |                |
| subjects affected / exposed      | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                | 0             | 0             | 0              |
| Urinary tract stoma complication |               |               |                |
| subjects affected / exposed      | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                | 0             | 0             | 0              |
| Cardiac disorders                |               |               |                |

|                             |               |               |                |
|-----------------------------|---------------|---------------|----------------|
| Atrial fibrillation         |               |               |                |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0             | 0             | 0              |
| Angina pectoris             |               |               |                |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0             | 0             | 0              |
| Palpitations                |               |               |                |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 1 / 12 (8.33%) |
| occurrences (all)           | 0             | 0             | 1              |
| Tachycardia                 |               |               |                |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0             | 0             | 0              |
| Sinus tachycardia           |               |               |                |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0             | 0             | 0              |
| Ventricular arrhythmia      |               |               |                |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0             | 0             | 0              |
| Nervous system disorders    |               |               |                |
| Ageusia                     |               |               |                |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0             | 0             | 0              |
| Agnosia                     |               |               |                |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0             | 0             | 0              |
| Amnesia                     |               |               |                |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0             | 0             | 0              |
| Cauda equina syndrome       |               |               |                |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0             | 0             | 0              |
| Disturbance in attention    |               |               |                |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0             | 0             | 0              |
| Dizziness                   |               |               |                |

|                               |                |                |                 |
|-------------------------------|----------------|----------------|-----------------|
| subjects affected / exposed   | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 0 / 12 (0.00%)  |
| occurrences (all)             | 0              | 0              | 0               |
| Dizziness postural            |                |                |                 |
| subjects affected / exposed   | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 0 / 12 (0.00%)  |
| occurrences (all)             | 0              | 0              | 0               |
| Headache                      |                |                |                 |
| subjects affected / exposed   | 1 / 2 (50.00%) | 1 / 2 (50.00%) | 2 / 12 (16.67%) |
| occurrences (all)             | 3              | 2              | 2               |
| Dysgeusia                     |                |                |                 |
| subjects affected / exposed   | 0 / 2 (0.00%)  | 1 / 2 (50.00%) | 3 / 12 (25.00%) |
| occurrences (all)             | 0              | 1              | 3               |
| Motor dysfunction             |                |                |                 |
| subjects affected / exposed   | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 0 / 12 (0.00%)  |
| occurrences (all)             | 0              | 0              | 0               |
| Neuropathy peripheral         |                |                |                 |
| subjects affected / exposed   | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 0 / 12 (0.00%)  |
| occurrences (all)             | 0              | 0              | 0               |
| Peripheral sensory neuropathy |                |                |                 |
| subjects affected / exposed   | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 0 / 12 (0.00%)  |
| occurrences (all)             | 0              | 0              | 0               |
| Paraesthesia                  |                |                |                 |
| subjects affected / exposed   | 1 / 2 (50.00%) | 0 / 2 (0.00%)  | 0 / 12 (0.00%)  |
| occurrences (all)             | 1              | 0              | 0               |
| Presyncope                    |                |                |                 |
| subjects affected / exposed   | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 1 / 12 (8.33%)  |
| occurrences (all)             | 0              | 0              | 1               |
| Radiculopathy                 |                |                |                 |
| subjects affected / exposed   | 1 / 2 (50.00%) | 0 / 2 (0.00%)  | 0 / 12 (0.00%)  |
| occurrences (all)             | 1              | 0              | 0               |
| Syncope                       |                |                |                 |
| subjects affected / exposed   | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 2 / 12 (16.67%) |
| occurrences (all)             | 0              | 0              | 2               |
| Somnolence                    |                |                |                 |
| subjects affected / exposed   | 1 / 2 (50.00%) | 0 / 2 (0.00%)  | 0 / 12 (0.00%)  |
| occurrences (all)             | 1              | 0              | 0               |
| Sciatica                      |                |                |                 |

|                                      |                |                |                 |
|--------------------------------------|----------------|----------------|-----------------|
| subjects affected / exposed          | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 1 / 12 (8.33%)  |
| occurrences (all)                    | 0              | 0              | 1               |
| Taste disorder                       |                |                |                 |
| subjects affected / exposed          | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 0 / 12 (0.00%)  |
| occurrences (all)                    | 0              | 0              | 0               |
| Blood and lymphatic system disorders |                |                |                 |
| Anaemia                              |                |                |                 |
| subjects affected / exposed          | 1 / 2 (50.00%) | 0 / 2 (0.00%)  | 6 / 12 (50.00%) |
| occurrences (all)                    | 1              | 0              | 8               |
| Coagulopathy                         |                |                |                 |
| subjects affected / exposed          | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 0 / 12 (0.00%)  |
| occurrences (all)                    | 0              | 0              | 0               |
| Eosinophilia                         |                |                |                 |
| subjects affected / exposed          | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 0 / 12 (0.00%)  |
| occurrences (all)                    | 0              | 0              | 0               |
| Lymph node haemorrhage               |                |                |                 |
| subjects affected / exposed          | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 0 / 12 (0.00%)  |
| occurrences (all)                    | 0              | 0              | 0               |
| Lymph node pain                      |                |                |                 |
| subjects affected / exposed          | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 0 / 12 (0.00%)  |
| occurrences (all)                    | 0              | 0              | 0               |
| Lymphadenopathy                      |                |                |                 |
| subjects affected / exposed          | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 0 / 12 (0.00%)  |
| occurrences (all)                    | 0              | 0              | 0               |
| Neutropenia                          |                |                |                 |
| subjects affected / exposed          | 0 / 2 (0.00%)  | 1 / 2 (50.00%) | 1 / 12 (8.33%)  |
| occurrences (all)                    | 0              | 1              | 1               |
| Lymphopenia                          |                |                |                 |
| subjects affected / exposed          | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 0 / 12 (0.00%)  |
| occurrences (all)                    | 0              | 0              | 0               |
| Thrombocytopenia                     |                |                |                 |
| subjects affected / exposed          | 0 / 2 (0.00%)  | 1 / 2 (50.00%) | 7 / 12 (58.33%) |
| occurrences (all)                    | 0              | 1              | 20              |
| Ear and labyrinth disorders          |                |                |                 |
| Ear congestion                       |                |                |                 |

|  |                     |                     |                     |
|--|---------------------|---------------------|---------------------|
| subjects affected / exposed<br>occurrences (all)   | 0 / 2 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0  | 0 / 12 (0.00%)<br>0 |
| Ear haemorrhage<br>subjects affected / exposed<br>occurrences (all)                                    | 0 / 2 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0  | 0 / 12 (0.00%)<br>0 |
| Ear pain<br>subjects affected / exposed<br>occurrences (all)   | 0 / 2 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0  | 0 / 12 (0.00%)<br>0 |
| Vertigo<br>subjects affected / exposed<br>occurrences (all)  | 0 / 2 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0  | 0 / 12 (0.00%)<br>0 |
| Eye disorders<br>Conjunctival haemorrhage<br>subjects affected / exposed<br>occurrences (all)          | 0 / 2 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0  | 0 / 12 (0.00%)<br>0 |
| Dry eye<br>subjects affected / exposed<br>occurrences (all)  | 0 / 2 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0  | 1 / 12 (8.33%)<br>1 |
| Vitreous haemorrhage<br>subjects affected / exposed<br>occurrences (all)                               | 0 / 2 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0  | 0 / 12 (0.00%)<br>0 |
| Vision blurred<br>subjects affected / exposed<br>occurrences (all)                                     | 0 / 2 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0  | 0 / 12 (0.00%)<br>0 |
| Periorbital oedema<br>subjects affected / exposed<br>occurrences (all)                                 | 0 / 2 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0  | 1 / 12 (8.33%)<br>1 |
| Gastrointestinal disorders<br>Abdominal pain upper<br>subjects affected / exposed<br>occurrences (all) | 1 / 2 (50.00%)<br>1 | 0 / 2 (0.00%)<br>0  | 1 / 12 (8.33%)<br>1 |
| Abdominal pain<br>subjects affected / exposed<br>occurrences (all)                                     | 0 / 2 (0.00%)<br>0  | 1 / 2 (50.00%)<br>1 | 1 / 12 (8.33%)<br>2 |
| Abdominal distension   |                     |                     |                     |

|                             |                |                 |                 |
|-----------------------------|----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 2 (0.00%)  | 0 / 2 (0.00%)   | 0 / 12 (0.00%)  |
| occurrences (all)           | 0              | 0               | 0               |
| Anal fissure                |                |                 |                 |
| subjects affected / exposed | 0 / 2 (0.00%)  | 0 / 2 (0.00%)   | 0 / 12 (0.00%)  |
| occurrences (all)           | 0              | 0               | 0               |
| Anal haemorrhage            |                |                 |                 |
| subjects affected / exposed | 0 / 2 (0.00%)  | 0 / 2 (0.00%)   | 0 / 12 (0.00%)  |
| occurrences (all)           | 0              | 0               | 0               |
| Aphthous ulcer              |                |                 |                 |
| subjects affected / exposed | 0 / 2 (0.00%)  | 0 / 2 (0.00%)   | 0 / 12 (0.00%)  |
| occurrences (all)           | 0              | 0               | 0               |
| Angular cheilitis           |                |                 |                 |
| subjects affected / exposed | 0 / 2 (0.00%)  | 0 / 2 (0.00%)   | 0 / 12 (0.00%)  |
| occurrences (all)           | 0              | 0               | 0               |
| Anal inflammation           |                |                 |                 |
| subjects affected / exposed | 0 / 2 (0.00%)  | 1 / 2 (50.00%)  | 0 / 12 (0.00%)  |
| occurrences (all)           | 0              | 1               | 0               |
| Ascites                     |                |                 |                 |
| subjects affected / exposed | 0 / 2 (0.00%)  | 0 / 2 (0.00%)   | 0 / 12 (0.00%)  |
| occurrences (all)           | 0              | 0               | 0               |
| Constipation                |                |                 |                 |
| subjects affected / exposed | 1 / 2 (50.00%) | 1 / 2 (50.00%)  | 4 / 12 (33.33%) |
| occurrences (all)           | 1              | 1               | 4               |
| Diarrhoea                   |                |                 |                 |
| subjects affected / exposed | 1 / 2 (50.00%) | 2 / 2 (100.00%) | 3 / 12 (25.00%) |
| occurrences (all)           | 1              | 3               | 6               |
| Dry mouth                   |                |                 |                 |
| subjects affected / exposed | 0 / 2 (0.00%)  | 0 / 2 (0.00%)   | 4 / 12 (33.33%) |
| occurrences (all)           | 0              | 0               | 4               |
| Dyspepsia                   |                |                 |                 |
| subjects affected / exposed | 0 / 2 (0.00%)  | 0 / 2 (0.00%)   | 1 / 12 (8.33%)  |
| occurrences (all)           | 0              | 0               | 1               |
| Dysphagia                   |                |                 |                 |
| subjects affected / exposed | 0 / 2 (0.00%)  | 0 / 2 (0.00%)   | 0 / 12 (0.00%)  |
| occurrences (all)           | 0              | 0               | 0               |
| Flatulence                  |                |                 |                 |



|                                    |                |               |                 |
|------------------------------------|----------------|---------------|-----------------|
| subjects affected / exposed        | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 1 / 12 (8.33%)  |
| occurrences (all)                  | 0              | 0             | 1               |
| Gastritis                          |                |               |                 |
| subjects affected / exposed        | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 12 (0.00%)  |
| occurrences (all)                  | 0              | 0             | 0               |
| Gastritis erosive                  |                |               |                 |
| subjects affected / exposed        | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 1 / 12 (8.33%)  |
| occurrences (all)                  | 0              | 0             | 1               |
| Gastrointestinal disorder          |                |               |                 |
| subjects affected / exposed        | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 12 (0.00%)  |
| occurrences (all)                  | 0              | 0             | 0               |
| Gastrooesophageal reflux disease   |                |               |                 |
| subjects affected / exposed        | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 12 (0.00%)  |
| occurrences (all)                  | 0              | 0             | 0               |
| Haemorrhoids                       |                |               |                 |
| subjects affected / exposed        | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 12 (0.00%)  |
| occurrences (all)                  | 0              | 0             | 0               |
| Lip dry                            |                |               |                 |
| subjects affected / exposed        | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 12 (0.00%)  |
| occurrences (all)                  | 0              | 0             | 0               |
| Melaena                            |                |               |                 |
| subjects affected / exposed        | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 12 (0.00%)  |
| occurrences (all)                  | 0              | 0             | 0               |
| Lower gastrointestinal haemorrhage |                |               |                 |
| subjects affected / exposed        | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 12 (0.00%)  |
| occurrences (all)                  | 0              | 0             | 0               |
| Nausea                             |                |               |                 |
| subjects affected / exposed        | 1 / 2 (50.00%) | 0 / 2 (0.00%) | 6 / 12 (50.00%) |
| occurrences (all)                  | 2              | 0             | 7               |
| Odynophagia                        |                |               |                 |
| subjects affected / exposed        | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 12 (0.00%)  |
| occurrences (all)                  | 0              | 0             | 0               |
| Oral mucosal erythema              |                |               |                 |
| subjects affected / exposed        | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 12 (0.00%)  |
| occurrences (all)                  | 0              | 0             | 0               |
| Retching                           |                |               |                 |

|  |                |                 |                 |
|--|----------------|-----------------|-----------------|
| subjects affected / exposed            | 0 / 2 (0.00%)  | 0 / 2 (0.00%)   | 0 / 12 (0.00%)  |
| occurrences (all)                      | 0              | 0               | 0               |
| Stomatitis                             |                |                 |                 |
| subjects affected / exposed            | 0 / 2 (0.00%)  | 2 / 2 (100.00%) | 0 / 12 (0.00%)  |
| occurrences (all)                      | 0              | 2               | 0               |
| Subileus                               |                |                 |                 |
| subjects affected / exposed            | 0 / 2 (0.00%)  | 0 / 2 (0.00%)   | 0 / 12 (0.00%)  |
| occurrences (all)                      | 0              | 0               | 0               |
| Toothache                              |                |                 |                 |
| subjects affected / exposed            | 0 / 2 (0.00%)  | 0 / 2 (0.00%)   | 0 / 12 (0.00%)  |
| occurrences (all)                      | 0              | 0               | 0               |
| Vomiting                               |                |                 |                 |
| subjects affected / exposed            | 1 / 2 (50.00%) | 0 / 2 (0.00%)   | 4 / 12 (33.33%) |
| occurrences (all)                      | 1              | 0               | 5               |
| Hepatobiliary disorders                |                |                 |                 |
| Cholangitis                            |                |                 |                 |
| subjects affected / exposed            | 0 / 2 (0.00%)  | 0 / 2 (0.00%)   | 0 / 12 (0.00%)  |
| occurrences (all)                      | 0              | 0               | 0               |
| Hepatic cytolysis                      |                |                 |                 |
| subjects affected / exposed            | 0 / 2 (0.00%)  | 0 / 2 (0.00%)   | 0 / 12 (0.00%)  |
| occurrences (all)                      | 0              | 0               | 0               |
| Hepatic pain                           |                |                 |                 |
| subjects affected / exposed            | 0 / 2 (0.00%)  | 0 / 2 (0.00%)   | 1 / 12 (8.33%)  |
| occurrences (all)                      | 0              | 0               | 1               |
| Skin and subcutaneous tissue disorders |                |                 |                 |
| Dermatitis psoriasiform                |                |                 |                 |
| subjects affected / exposed            | 0 / 2 (0.00%)  | 0 / 2 (0.00%)   | 0 / 12 (0.00%)  |
| occurrences (all)                      | 0              | 0               | 0               |
| Dermatitis acneiform                   |                |                 |                 |
| subjects affected / exposed            | 0 / 2 (0.00%)  | 0 / 2 (0.00%)   | 2 / 12 (16.67%) |
| occurrences (all)                      | 0              | 0               | 3               |
| Dry skin                               |                |                 |                 |
| subjects affected / exposed            | 0 / 2 (0.00%)  | 0 / 2 (0.00%)   | 0 / 12 (0.00%)  |
| occurrences (all)                      | 0              | 0               | 0               |
| Intertrigo                             |                |                 |                 |

|                             |               |               |                |
|-----------------------------|---------------|---------------|----------------|
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0             | 0             | 0              |
| Macule                      |               |               |                |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0             | 0             | 0              |
| Night sweats                |               |               |                |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0             | 0             | 0              |
| Eczema                      |               |               |                |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0             | 0             | 0              |
| Erythema                    |               |               |                |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 1 / 12 (8.33%) |
| occurrences (all)           | 0             | 0             | 1              |
| Prurigo                     |               |               |                |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0             | 0             | 0              |
| Pruritus                    |               |               |                |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 1 / 12 (8.33%) |
| occurrences (all)           | 0             | 0             | 1              |
| Psoriasis                   |               |               |                |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0             | 0             | 0              |
| Petechiae                   |               |               |                |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0             | 0             | 0              |
| Skin ulcer                  |               |               |                |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0             | 0             | 0              |
| Rash                        |               |               |                |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0             | 0             | 0              |
| Rash maculo-papular         |               |               |                |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0             | 0             | 0              |
| Purpura                     |               |               |                |

|   |               |                |                |
|---|---------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 0 / 12 (0.00%) |
| occurrences (all)                               | 0             | 0              | 0              |
| Urticaria                                       |               |                |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 0 / 12 (0.00%) |
| occurrences (all)                               | 0             | 0              | 0              |
| Renal and urinary disorders                     |               |                |                |
| Dysuria   |               |                |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 0 / 12 (0.00%) |
| occurrences (all)                               | 0             | 0              | 0              |
| Haematuria                                      |               |                |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 0 / 12 (0.00%) |
| occurrences (all)                               | 0             | 0              | 0              |
| Pollakiuria                                     |               |                |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 0 / 12 (0.00%) |
| occurrences (all)                               | 0             | 0              | 0              |
| Urinary tract pain                              |               |                |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 0 / 12 (0.00%) |
| occurrences (all)                               | 0             | 0              | 0              |
| Urinary retention                               |               |                |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 0 / 12 (0.00%) |
| occurrences (all)                               | 0             | 0              | 0              |
| Renal failure                                   |               |                |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 0 / 12 (0.00%) |
| occurrences (all)                               | 0             | 0              | 0              |
| Endocrine disorders                             |               |                |                |
| Hyperthyroidism                                 |               |                |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 0 / 12 (0.00%) |
| occurrences (all)                               | 0             | 0              | 0              |
| Musculoskeletal and connective tissue disorders |               |                |                |
| Arthralgia                                      |               |                |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 1 / 2 (50.00%) | 0 / 12 (0.00%) |
| occurrences (all)                               | 0             | 2              | 0              |
| Back pain                                       |               |                |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 1 / 12 (8.33%) |
| occurrences (all)                               | 0             | 0              | 2              |
| Bone pain                                       |               |                |                |

|                             |               |                |                |
|-----------------------------|---------------|----------------|----------------|
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 0 / 12 (0.00%) |
| occurrences (all)           | 0             | 0              | 0              |
| Flank pain                  |               |                |                |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 0 / 12 (0.00%) |
| occurrences (all)           | 0             | 0              | 0              |
| Groin pain                  |               |                |                |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 0 / 12 (0.00%) |
| occurrences (all)           | 0             | 0              | 0              |
| Muscular weakness           |               |                |                |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 0 / 12 (0.00%) |
| occurrences (all)           | 0             | 0              | 0              |
| Muscle spasms               |               |                |                |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 1 / 12 (8.33%) |
| occurrences (all)           | 0             | 0              | 1              |
| Myalgia                     |               |                |                |
| subjects affected / exposed | 0 / 2 (0.00%) | 1 / 2 (50.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0             | 2              | 0              |
| Neck pain                   |               |                |                |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 0 / 12 (0.00%) |
| occurrences (all)           | 0             | 0              | 0              |
| Pain in extremity           |               |                |                |
| subjects affected / exposed | 0 / 2 (0.00%) | 1 / 2 (50.00%) | 1 / 12 (8.33%) |
| occurrences (all)           | 0             | 1              | 1              |
| Pubic pain                  |               |                |                |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 0 / 12 (0.00%) |
| occurrences (all)           | 0             | 0              | 0              |
| Infections and infestations |               |                |                |
| Bronchitis                  |               |                |                |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 0 / 12 (0.00%) |
| occurrences (all)           | 0             | 0              | 0              |
| Bronchitis viral            |               |                |                |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 0 / 12 (0.00%) |
| occurrences (all)           | 0             | 0              | 0              |
| Clostridial infection       |               |                |                |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 0 / 12 (0.00%) |
| occurrences (all)           | 0             | 0              | 0              |

|                                     |               |               |                |
|-------------------------------------|---------------|---------------|----------------|
| Clostridium difficile colitis       |               |               |                |
| subjects affected / exposed         | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                   | 0             | 0             | 0              |
| Conjunctivitis                      |               |               |                |
| subjects affected / exposed         | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                   | 0             | 0             | 0              |
| Erysipelas                          |               |               |                |
| subjects affected / exposed         | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                   | 0             | 0             | 0              |
| Diverticulitis                      |               |               |                |
| subjects affected / exposed         | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                   | 0             | 0             | 0              |
| Cystitis                            |               |               |                |
| subjects affected / exposed         | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 1 / 12 (8.33%) |
| occurrences (all)                   | 0             | 0             | 1              |
| Gastroenteritis                     |               |               |                |
| subjects affected / exposed         | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                   | 0             | 0             | 0              |
| Folliculitis                        |               |               |                |
| subjects affected / exposed         | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                   | 0             | 0             | 0              |
| Escherichia urinary tract infection |               |               |                |
| subjects affected / exposed         | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                   | 0             | 0             | 0              |
| Genital herpes simplex              |               |               |                |
| subjects affected / exposed         | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                   | 0             | 0             | 0              |
| Genital infection fungal            |               |               |                |
| subjects affected / exposed         | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                   | 0             | 0             | 0              |
| Herpes dermatitis                   |               |               |                |
| subjects affected / exposed         | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                   | 0             | 0             | 0              |
| Impetigo                            |               |               |                |
| subjects affected / exposed         | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 12 (0.00%) |
| occurrences (all)                   | 0             | 0             | 0              |

|                                       |                |                |                |
|---------------------------------------|----------------|----------------|----------------|
| Herpes zoster                         |                |                |                |
| subjects affected / exposed           | 0 / 2 (0.00%)  | 1 / 2 (50.00%) | 1 / 12 (8.33%) |
| occurrences (all)                     | 0              | 1              | 1              |
| Influenza                             |                |                |                |
| subjects affected / exposed           | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 0 / 12 (0.00%) |
| occurrences (all)                     | 0              | 0              | 0              |
| Infection                             |                |                |                |
| subjects affected / exposed           | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 0 / 12 (0.00%) |
| occurrences (all)                     | 0              | 0              | 0              |
| Nasopharyngitis                       |                |                |                |
| subjects affected / exposed           | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 0 / 12 (0.00%) |
| occurrences (all)                     | 0              | 0              | 0              |
| Oesophageal infection                 |                |                |                |
| subjects affected / exposed           | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 0 / 12 (0.00%) |
| occurrences (all)                     | 0              | 0              | 0              |
| Pharyngitis                           |                |                |                |
| subjects affected / exposed           | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 0 / 12 (0.00%) |
| occurrences (all)                     | 0              | 0              | 0              |
| Oral herpes                           |                |                |                |
| subjects affected / exposed           | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 1 / 12 (8.33%) |
| occurrences (all)                     | 0              | 0              | 1              |
| Pneumonia                             |                |                |                |
| subjects affected / exposed           | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 1 / 12 (8.33%) |
| occurrences (all)                     | 0              | 0              | 1              |
| Rash pustular                         |                |                |                |
| subjects affected / exposed           | 0 / 2 (0.00%)  | 1 / 2 (50.00%) | 0 / 12 (0.00%) |
| occurrences (all)                     | 0              | 2              | 0              |
| Respiratory tract infection           |                |                |                |
| subjects affected / exposed           | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 0 / 12 (0.00%) |
| occurrences (all)                     | 0              | 0              | 0              |
| Respiratory tract infection bacterial |                |                |                |
| subjects affected / exposed           | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 0 / 12 (0.00%) |
| occurrences (all)                     | 0              | 0              | 0              |
| Sinusitis                             |                |                |                |
| subjects affected / exposed           | 1 / 2 (50.00%) | 0 / 2 (0.00%)  | 0 / 12 (0.00%) |
| occurrences (all)                     | 1              | 0              | 0              |

|  |                     |                      |                      |
|--|---------------------|----------------------|----------------------|
| Tooth abscess<br>subjects affected / exposed<br>occurrences (all)                                  | 0 / 2 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0   | 0 / 12 (0.00%)<br>0  |
| Tooth infection<br>subjects affected / exposed<br>occurrences (all)                                | 0 / 2 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0   | 0 / 12 (0.00%)<br>0  |
| Tracheitis<br>subjects affected / exposed<br>occurrences (all)                                     | 0 / 2 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0   | 0 / 12 (0.00%)<br>0  |
| Upper respiratory tract infection<br>subjects affected / exposed<br>occurrences (all)              | 1 / 2 (50.00%)<br>1 | 0 / 2 (0.00%)<br>0   | 0 / 12 (0.00%)<br>0  |
| Urinary tract infection enterococcal<br>subjects affected / exposed<br>occurrences (all)           | 0 / 2 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0   | 0 / 12 (0.00%)<br>0  |
| Urinary tract infection<br>subjects affected / exposed<br>occurrences (all)                        | 0 / 2 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0   | 1 / 12 (8.33%)<br>1  |
| Mucosal infection<br>subjects affected / exposed<br>occurrences (all)                              | 0 / 2 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0   | 0 / 12 (0.00%)<br>0  |
| Stoma site infection<br>subjects affected / exposed<br>occurrences (all)                           | 0 / 2 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0   | 0 / 12 (0.00%)<br>0  |
| Metabolism and nutrition disorders<br>Acidosis<br>subjects affected / exposed<br>occurrences (all) | 0 / 2 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0   | 0 / 12 (0.00%)<br>0  |
| Decreased appetite<br>subjects affected / exposed<br>occurrences (all)                             | 1 / 2 (50.00%)<br>1 | 2 / 2 (100.00%)<br>3 | 6 / 12 (50.00%)<br>7 |
| Cell death<br>subjects affected / exposed<br>occurrences (all)                                     | 0 / 2 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0   | 0 / 12 (0.00%)<br>0  |
| Dehydration  |                     |                      |                      |



|                             |               |                |                |
|-----------------------------|---------------|----------------|----------------|
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 0 / 12 (0.00%) |
| occurrences (all)           | 0             | 0              | 0              |
| Fluid retention             |               |                |                |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 0 / 12 (0.00%) |
| occurrences (all)           | 0             | 0              | 0              |
| Folate deficiency           |               |                |                |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 0 / 12 (0.00%) |
| occurrences (all)           | 0             | 0              | 0              |
| Gout                        |               |                |                |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 0 / 12 (0.00%) |
| occurrences (all)           | 0             | 0              | 0              |
| Hypercalcaemia              |               |                |                |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 0 / 12 (0.00%) |
| occurrences (all)           | 0             | 0              | 0              |
| Hyperkalaemia               |               |                |                |
| subjects affected / exposed | 0 / 2 (0.00%) | 1 / 2 (50.00%) | 0 / 12 (0.00%) |
| occurrences (all)           | 0             | 1              | 0              |
| Hyperglycaemia              |               |                |                |
| subjects affected / exposed | 0 / 2 (0.00%) | 1 / 2 (50.00%) | 1 / 12 (8.33%) |
| occurrences (all)           | 0             | 1              | 3              |
| Hyperphosphataemia          |               |                |                |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 0 / 12 (0.00%) |
| occurrences (all)           | 0             | 0              | 0              |
| Hypoalbuminaemia            |               |                |                |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 0 / 12 (0.00%) |
| occurrences (all)           | 0             | 0              | 0              |
| Hypocalcaemia               |               |                |                |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 1 / 12 (8.33%) |
| occurrences (all)           | 0             | 0              | 1              |
| Hypokalaemia                |               |                |                |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 1 / 12 (8.33%) |
| occurrences (all)           | 0             | 0              | 1              |
| Hypomagnesaemia             |               |                |                |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 0 / 12 (0.00%) |
| occurrences (all)           | 0             | 0              | 0              |
| Hyponatraemia               |               |                |                |

|                             |               |                 |                |
|-----------------------------|---------------|-----------------|----------------|
| subjects affected / exposed | 0 / 2 (0.00%) | 1 / 2 (50.00%)  | 0 / 12 (0.00%) |
| occurrences (all)           | 0             | 1               | 0              |
| Hypophosphataemia           |               |                 |                |
| subjects affected / exposed | 0 / 2 (0.00%) | 2 / 2 (100.00%) | 1 / 12 (8.33%) |
| occurrences (all)           | 0             | 3               | 1              |
| Malnutrition                |               |                 |                |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 2 (0.00%)   | 0 / 12 (0.00%) |
| occurrences (all)           | 0             | 0               | 0              |

| <b>Non-serious adverse events</b>                                   | Phase Ia - Schedule B: 1.5 mg BI 894999 (DLBCL patients) | Phase Ib - Schedule B: 2.5 mg BI 894999 (SCLC patients) | Phase Ia - Schedule C: BI 894999 5/2.5 mg (DLBCL patients) |
|---|--|---|--|
| Total subjects affected by non-serious adverse events               |  |   |  |
| subjects affected / exposed   | 8 / 8 (100.00%)  | 3 / 3 (100.00%)   | 2 / 2 (100.00%)  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |  |   |  |
| Tumour pain   |  |   |  |
| subjects affected / exposed   | 0 / 8 (0.00%)  | 0 / 3 (0.00%)   | 0 / 2 (0.00%)  |
| occurrences (all)   | 0  | 0   | 0  |
| Vascular disorders  |  |   |  |
| Hypotension   |  |   |  |
| subjects affected / exposed   | 0 / 8 (0.00%)  | 0 / 3 (0.00%)   | 1 / 2 (50.00%)   |
| occurrences (all)   | 0  | 0   | 1  |
| Hypertension  |  |   |  |
| subjects affected / exposed   | 0 / 8 (0.00%)  | 0 / 3 (0.00%)   | 0 / 2 (0.00%)  |
| occurrences (all)   | 0  | 0   | 0  |
| Haematoma   |  |   |  |
| subjects affected / exposed   | 0 / 8 (0.00%)  | 0 / 3 (0.00%)   | 0 / 2 (0.00%)  |
| occurrences (all)   | 0  | 0   | 0  |
| Orthostatic hypotension   |  |   |  |
| subjects affected / exposed   | 0 / 8 (0.00%)  | 0 / 3 (0.00%)   | 0 / 2 (0.00%)  |
| occurrences (all)   | 0  | 0   | 0  |
| Pallor  |  |   |  |
| subjects affected / exposed   | 0 / 8 (0.00%)  | 0 / 3 (0.00%)   | 0 / 2 (0.00%)  |
| occurrences (all)   | 0  | 0   | 0  |
| General disorders and administration site conditions                |  |   |  |

|                                       |                |                |                |
|---------------------------------------|----------------|----------------|----------------|
| Chest discomfort                      |                |                |                |
| subjects affected / exposed           | 0 / 8 (0.00%)  | 0 / 3 (0.00%)  | 0 / 2 (0.00%)  |
| occurrences (all)                     | 0              | 0              | 0              |
| Asthenia                              |                |                |                |
| subjects affected / exposed           | 2 / 8 (25.00%) | 0 / 3 (0.00%)  | 1 / 2 (50.00%) |
| occurrences (all)                     | 3              | 0              | 1              |
| Chest pain                            |                |                |                |
| subjects affected / exposed           | 1 / 8 (12.50%) | 0 / 3 (0.00%)  | 0 / 2 (0.00%)  |
| occurrences (all)                     | 1              | 0              | 0              |
| Fatigue                               |                |                |                |
| subjects affected / exposed           | 0 / 8 (0.00%)  | 1 / 3 (33.33%) | 0 / 2 (0.00%)  |
| occurrences (all)                     | 0              | 3              | 0              |
| Facial pain                           |                |                |                |
| subjects affected / exposed           | 0 / 8 (0.00%)  | 0 / 3 (0.00%)  | 0 / 2 (0.00%)  |
| occurrences (all)                     | 0              | 0              | 0              |
| Chills                                |                |                |                |
| subjects affected / exposed           | 0 / 8 (0.00%)  | 0 / 3 (0.00%)  | 0 / 2 (0.00%)  |
| occurrences (all)                     | 0              | 0              | 0              |
| Gait disturbance                      |                |                |                |
| subjects affected / exposed           | 0 / 8 (0.00%)  | 0 / 3 (0.00%)  | 1 / 2 (50.00%) |
| occurrences (all)                     | 0              | 0              | 1              |
| General physical health deterioration |                |                |                |
| subjects affected / exposed           | 0 / 8 (0.00%)  | 0 / 3 (0.00%)  | 0 / 2 (0.00%)  |
| occurrences (all)                     | 0              | 0              | 0              |
| Generalised oedema                    |                |                |                |
| subjects affected / exposed           | 0 / 8 (0.00%)  | 0 / 3 (0.00%)  | 0 / 2 (0.00%)  |
| occurrences (all)                     | 0              | 0              | 0              |
| Malaise                               |                |                |                |
| subjects affected / exposed           | 0 / 8 (0.00%)  | 0 / 3 (0.00%)  | 0 / 2 (0.00%)  |
| occurrences (all)                     | 0              | 0              | 0              |
| Hypothermia                           |                |                |                |
| subjects affected / exposed           | 0 / 8 (0.00%)  | 0 / 3 (0.00%)  | 0 / 2 (0.00%)  |
| occurrences (all)                     | 0              | 0              | 0              |
| Oedema peripheral                     |                |                |                |
| subjects affected / exposed           | 0 / 8 (0.00%)  | 1 / 3 (33.33%) | 0 / 2 (0.00%)  |
| occurrences (all)                     | 0              | 1              | 0              |

|  |                     |                    |                     |
|--|---------------------|--------------------|---------------------|
| Non-cardiac chest pain<br>subjects affected / exposed<br>occurrences (all)   | 0 / 8 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0 | 0 / 2 (0.00%)<br>0  |
| Pain<br>subjects affected / exposed<br>occurrences (all)   | 0 / 8 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0 | 0 / 2 (0.00%)<br>0  |
| Pyrexia<br>subjects affected / exposed<br>occurrences (all)  | 1 / 8 (12.50%)<br>3 | 0 / 3 (0.00%)<br>0 | 1 / 2 (50.00%)<br>1 |
| Peripheral swelling<br>subjects affected / exposed<br>occurrences (all)  | 0 / 8 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0 | 0 / 2 (0.00%)<br>0  |
| Immune system disorders<br>Hypersensitivity<br>subjects affected / exposed<br>occurrences (all)                      | 0 / 8 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0 | 0 / 2 (0.00%)<br>0  |
| Iodine allergy<br>subjects affected / exposed<br>occurrences (all)   | 0 / 8 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0 | 0 / 2 (0.00%)<br>0  |
| Reproductive system and breast disorders<br>Erectile dysfunction<br>subjects affected / exposed<br>occurrences (all) | 0 / 8 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0 | 0 / 2 (0.00%)<br>0  |
| Heavy menstrual bleeding<br>subjects affected / exposed<br>occurrences (all)   | 0 / 8 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0 | 0 / 2 (0.00%)<br>0  |
| Oedema genital<br>subjects affected / exposed<br>occurrences (all)   | 0 / 8 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0 | 0 / 2 (0.00%)<br>0  |
| Perineal pain<br>subjects affected / exposed<br>occurrences (all)  | 0 / 8 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0 | 0 / 2 (0.00%)<br>0  |
| Scrotal oedema<br>subjects affected / exposed<br>occurrences (all)   | 0 / 8 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0 | 0 / 2 (0.00%)<br>0  |
| Testicular pain  |                     |                    |                     |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 8 (0.00%)  | 0 / 3 (0.00%)  | 0 / 2 (0.00%)  |
| occurrences (all)                               | 0              | 0              | 0              |
| Vulvovaginal discomfort                         |                |                |                |
| subjects affected / exposed                     | 0 / 8 (0.00%)  | 0 / 3 (0.00%)  | 0 / 2 (0.00%)  |
| occurrences (all)                               | 0              | 0              | 0              |
| Vaginal haemorrhage                             |                |                |                |
| subjects affected / exposed                     | 0 / 8 (0.00%)  | 0 / 3 (0.00%)  | 0 / 2 (0.00%)  |
| occurrences (all)                               | 0              | 0              | 0              |
| Respiratory, thoracic and mediastinal disorders |                |                |                |
| Atelectasis                                     |                |                |                |
| subjects affected / exposed                     | 0 / 8 (0.00%)  | 0 / 3 (0.00%)  | 0 / 2 (0.00%)  |
| occurrences (all)                               | 0              | 0              | 0              |
| Dysphonia                                       |                |                |                |
| subjects affected / exposed                     | 0 / 8 (0.00%)  | 0 / 3 (0.00%)  | 0 / 2 (0.00%)  |
| occurrences (all)                               | 0              | 0              | 0              |
| Cough   |                |                |                |
| subjects affected / exposed                     | 1 / 8 (12.50%) | 2 / 3 (66.67%) | 0 / 2 (0.00%)  |
| occurrences (all)                               | 1              | 2              | 0              |
| Dyspnoea  |                |                |                |
| subjects affected / exposed                     | 1 / 8 (12.50%) | 2 / 3 (66.67%) | 0 / 2 (0.00%)  |
| occurrences (all)                               | 1              | 2              | 0              |
| Dyspnoea exertional                             |                |                |                |
| subjects affected / exposed                     | 0 / 8 (0.00%)  | 0 / 3 (0.00%)  | 0 / 2 (0.00%)  |
| occurrences (all)                               | 0              | 0              | 0              |
| Epistaxis                                       |                |                |                |
| subjects affected / exposed                     | 0 / 8 (0.00%)  | 0 / 3 (0.00%)  | 1 / 2 (50.00%) |
| occurrences (all)                               | 0              | 0              | 1              |
| Laryngeal inflammation                          |                |                |                |
| subjects affected / exposed                     | 0 / 8 (0.00%)  | 1 / 3 (33.33%) | 0 / 2 (0.00%)  |
| occurrences (all)                               | 0              | 1              | 0              |
| Haemoptysis                                     |                |                |                |
| subjects affected / exposed                     | 0 / 8 (0.00%)  | 0 / 3 (0.00%)  | 0 / 2 (0.00%)  |
| occurrences (all)                               | 0              | 0              | 0              |
| Nasal discomfort                                |                |                |                |

|                              |                |               |               |
|------------------------------|----------------|---------------|---------------|
| subjects affected / exposed  | 0 / 8 (0.00%)  | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all)            | 0              | 0             | 0             |
| Oropharyngeal pain           |                |               |               |
| subjects affected / exposed  | 0 / 8 (0.00%)  | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all)            | 0              | 0             | 0             |
| Pharyngeal inflammation      |                |               |               |
| subjects affected / exposed  | 0 / 8 (0.00%)  | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all)            | 0              | 0             | 0             |
| Pleural effusion             |                |               |               |
| subjects affected / exposed  | 1 / 8 (12.50%) | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all)            | 1              | 0             | 0             |
| Pleuritic pain               |                |               |               |
| subjects affected / exposed  | 1 / 8 (12.50%) | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all)            | 1              | 0             | 0             |
| Productive cough             |                |               |               |
| subjects affected / exposed  | 0 / 8 (0.00%)  | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all)            | 0              | 0             | 0             |
| Rhinorrhoea                  |                |               |               |
| subjects affected / exposed  | 1 / 8 (12.50%) | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all)            | 2              | 0             | 0             |
| Respiratory tract congestion |                |               |               |
| subjects affected / exposed  | 0 / 8 (0.00%)  | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all)            | 0              | 0             | 0             |
| Wheezing                     |                |               |               |
| subjects affected / exposed  | 0 / 8 (0.00%)  | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all)            | 0              | 0             | 0             |
| Psychiatric disorders        |                |               |               |
| Affective disorder           |                |               |               |
| subjects affected / exposed  | 0 / 8 (0.00%)  | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all)            | 0              | 0             | 0             |
| Agitation                    |                |               |               |
| subjects affected / exposed  | 0 / 8 (0.00%)  | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all)            | 0              | 0             | 0             |
| Anxiety                      |                |               |               |
| subjects affected / exposed  | 0 / 8 (0.00%)  | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all)            | 0              | 0             | 0             |

|   |               |                |                |
|---|---------------|----------------|----------------|
| Confusional state                               |               |                |                |
| subjects affected / exposed                     | 0 / 8 (0.00%) | 0 / 3 (0.00%)  | 0 / 2 (0.00%)  |
| occurrences (all)                               | 0             | 0              | 0              |
| Depression                                      |               |                |                |
| subjects affected / exposed                     | 0 / 8 (0.00%) | 0 / 3 (0.00%)  | 0 / 2 (0.00%)  |
| occurrences (all)                               | 0             | 0              | 0              |
| Insomnia  |               |                |                |
| subjects affected / exposed                     | 0 / 8 (0.00%) | 0 / 3 (0.00%)  | 0 / 2 (0.00%)  |
| occurrences (all)                               | 0             | 0              | 0              |
| Hallucination                                   |               |                |                |
| subjects affected / exposed                     | 0 / 8 (0.00%) | 0 / 3 (0.00%)  | 0 / 2 (0.00%)  |
| occurrences (all)                               | 0             | 0              | 0              |
| Personality change                              |               |                |                |
| subjects affected / exposed                     | 0 / 8 (0.00%) | 0 / 3 (0.00%)  | 0 / 2 (0.00%)  |
| occurrences (all)                               | 0             | 0              | 0              |
| Sleep disorder                                  |               |                |                |
| subjects affected / exposed                     | 0 / 8 (0.00%) | 0 / 3 (0.00%)  | 0 / 2 (0.00%)  |
| occurrences (all)                               | 0             | 0              | 0              |
| Investigations                                  |               |                |                |
| Activated partial thromboplastin time prolonged |               |                |                |
| subjects affected / exposed                     | 0 / 8 (0.00%) | 0 / 3 (0.00%)  | 0 / 2 (0.00%)  |
| occurrences (all)                               | 0             | 0              | 0              |
| Activated partial thromboplastin time shortened |               |                |                |
| subjects affected / exposed                     | 0 / 8 (0.00%) | 0 / 3 (0.00%)  | 0 / 2 (0.00%)  |
| occurrences (all)                               | 0             | 0              | 0              |
| Alanine aminotransferase increased              |               |                |                |
| subjects affected / exposed                     | 0 / 8 (0.00%) | 1 / 3 (33.33%) | 1 / 2 (50.00%) |
| occurrences (all)                               | 0             | 1              | 1              |
| Aspartate aminotransferase increased            |               |                |                |
| subjects affected / exposed                     | 0 / 8 (0.00%) | 1 / 3 (33.33%) | 1 / 2 (50.00%) |
| occurrences (all)                               | 0             | 1              | 1              |
| Blood alkaline phosphatase increased            |               |                |                |
| subjects affected / exposed                     | 0 / 8 (0.00%) | 1 / 3 (33.33%) | 0 / 2 (0.00%)  |
| occurrences (all)                               | 0             | 1              | 0              |
| Blood antidiuretic hormone                      |               |                |                |

|  |                |               |                |
|--|----------------|---------------|----------------|
| decreased                              |                |               |                |
| subjects affected / exposed            | 0 / 8 (0.00%)  | 0 / 3 (0.00%) | 0 / 2 (0.00%)  |
| occurrences (all)                      | 0              | 0             | 0              |
| Blood bilirubin increased              |                |               |                |
| subjects affected / exposed            | 0 / 8 (0.00%)  | 0 / 3 (0.00%) | 0 / 2 (0.00%)  |
| occurrences (all)                      | 0              | 0             | 0              |
| Blood creatine phosphokinase increased |                |               |                |
| subjects affected / exposed            | 0 / 8 (0.00%)  | 0 / 3 (0.00%) | 0 / 2 (0.00%)  |
| occurrences (all)                      | 0              | 0             | 0              |
| Blood creatinine increased             |                |               |                |
| subjects affected / exposed            | 0 / 8 (0.00%)  | 0 / 3 (0.00%) | 0 / 2 (0.00%)  |
| occurrences (all)                      | 0              | 0             | 0              |
| Blood magnesium decreased              |                |               |                |
| subjects affected / exposed            | 0 / 8 (0.00%)  | 0 / 3 (0.00%) | 0 / 2 (0.00%)  |
| occurrences (all)                      | 0              | 0             | 0              |
| Blood glucose increased                |                |               |                |
| subjects affected / exposed            | 0 / 8 (0.00%)  | 0 / 3 (0.00%) | 0 / 2 (0.00%)  |
| occurrences (all)                      | 0              | 0             | 0              |
| C-reactive protein increased           |                |               |                |
| subjects affected / exposed            | 0 / 8 (0.00%)  | 0 / 3 (0.00%) | 0 / 2 (0.00%)  |
| occurrences (all)                      | 0              | 0             | 0              |
| Cardiac murmur                         |                |               |                |
| subjects affected / exposed            | 1 / 8 (12.50%) | 0 / 3 (0.00%) | 0 / 2 (0.00%)  |
| occurrences (all)                      | 1              | 0             | 0              |
| Cortisol increased                     |                |               |                |
| subjects affected / exposed            | 0 / 8 (0.00%)  | 0 / 3 (0.00%) | 0 / 2 (0.00%)  |
| occurrences (all)                      | 0              | 0             | 0              |
| Echocardiogram abnormal                |                |               |                |
| subjects affected / exposed            | 0 / 8 (0.00%)  | 0 / 3 (0.00%) | 1 / 2 (50.00%) |
| occurrences (all)                      | 0              | 0             | 1              |
| Electrocardiogram PR prolongation      |                |               |                |
| subjects affected / exposed            | 0 / 8 (0.00%)  | 0 / 3 (0.00%) | 0 / 2 (0.00%)  |
| occurrences (all)                      | 0              | 0             | 0              |
| Ejection fraction decreased            |                |               |                |



|  |               |                |                |
|--|---------------|----------------|----------------|
| subjects affected / exposed              | 0 / 8 (0.00%) | 0 / 3 (0.00%)  | 0 / 2 (0.00%)  |
| occurrences (all)                        | 0             | 0              | 0              |
| Electrocardiogram ST segment elevation   |               |                |                |
| subjects affected / exposed              | 0 / 8 (0.00%) | 0 / 3 (0.00%)  | 0 / 2 (0.00%)  |
| occurrences (all)                        | 0             | 0              | 0              |
| Gamma-glutamyltransferase increased      |               |                |                |
| subjects affected / exposed              | 0 / 8 (0.00%) | 0 / 3 (0.00%)  | 0 / 2 (0.00%)  |
| occurrences (all)                        | 0             | 0              | 0              |
| Electrocardiogram T wave inversion       |               |                |                |
| subjects affected / exposed              | 0 / 8 (0.00%) | 0 / 3 (0.00%)  | 0 / 2 (0.00%)  |
| occurrences (all)                        | 0             | 0              | 0              |
| International normalised ratio increased |               |                |                |
| subjects affected / exposed              | 0 / 8 (0.00%) | 0 / 3 (0.00%)  | 0 / 2 (0.00%)  |
| occurrences (all)                        | 0             | 0              | 0              |
| Lymphocyte count decreased               |               |                |                |
| subjects affected / exposed              | 0 / 8 (0.00%) | 0 / 3 (0.00%)  | 0 / 2 (0.00%)  |
| occurrences (all)                        | 0             | 0              | 0              |
| Neutrophil count decreased               |               |                |                |
| subjects affected / exposed              | 0 / 8 (0.00%) | 0 / 3 (0.00%)  | 0 / 2 (0.00%)  |
| occurrences (all)                        | 0             | 0              | 0              |
| Platelet count decreased                 |               |                |                |
| subjects affected / exposed              | 0 / 8 (0.00%) | 0 / 3 (0.00%)  | 1 / 2 (50.00%) |
| occurrences (all)                        | 0             | 0              | 2              |
| Prothrombin level decreased              |               |                |                |
| subjects affected / exposed              | 0 / 8 (0.00%) | 0 / 3 (0.00%)  | 0 / 2 (0.00%)  |
| occurrences (all)                        | 0             | 0              | 0              |
| Troponin I increased                     |               |                |                |
| subjects affected / exposed              | 0 / 8 (0.00%) | 0 / 3 (0.00%)  | 1 / 2 (50.00%) |
| occurrences (all)                        | 0             | 0              | 1              |
| Troponin T increased                     |               |                |                |
| subjects affected / exposed              | 0 / 8 (0.00%) | 1 / 3 (33.33%) | 0 / 2 (0.00%)  |
| occurrences (all)                        | 0             | 1              | 0              |
| Troponin increased                       |               |                |                |

|  |                |               |                |
|--|----------------|---------------|----------------|
| subjects affected / exposed                    | 2 / 8 (25.00%) | 0 / 3 (0.00%) | 1 / 2 (50.00%) |
| occurrences (all)                              | 3              | 0             | 1              |
| Urine output decreased                         |                |               |                |
| subjects affected / exposed                    | 0 / 8 (0.00%)  | 0 / 3 (0.00%) | 0 / 2 (0.00%)  |
| occurrences (all)                              | 0              | 0             | 0              |
| Weight decreased                               |                |               |                |
| subjects affected / exposed                    | 1 / 8 (12.50%) | 0 / 3 (0.00%) | 0 / 2 (0.00%)  |
| occurrences (all)                              | 1              | 0             | 0              |
| White blood cell count decreased               |                |               |                |
| subjects affected / exposed                    | 0 / 8 (0.00%)  | 0 / 3 (0.00%) | 0 / 2 (0.00%)  |
| occurrences (all)                              | 0              | 0             | 0              |
| Injury, poisoning and procedural complications |                |               |                |
| Contusion                                      |                |               |                |
| subjects affected / exposed                    | 0 / 8 (0.00%)  | 0 / 3 (0.00%) | 0 / 2 (0.00%)  |
| occurrences (all)                              | 0              | 0             | 0              |
| Face injury                                    |                |               |                |
| subjects affected / exposed                    | 0 / 8 (0.00%)  | 0 / 3 (0.00%) | 0 / 2 (0.00%)  |
| occurrences (all)                              | 0              | 0             | 0              |
| Infusion related reaction                      |                |               |                |
| subjects affected / exposed                    | 0 / 8 (0.00%)  | 0 / 3 (0.00%) | 0 / 2 (0.00%)  |
| occurrences (all)                              | 0              | 0             | 0              |
| Limb injury                                    |                |               |                |
| subjects affected / exposed                    | 0 / 8 (0.00%)  | 0 / 3 (0.00%) | 0 / 2 (0.00%)  |
| occurrences (all)                              | 0              | 0             | 0              |
| Muscle rupture                                 |                |               |                |
| subjects affected / exposed                    | 0 / 8 (0.00%)  | 0 / 3 (0.00%) | 0 / 2 (0.00%)  |
| occurrences (all)                              | 0              | 0             | 0              |
| Overdose                                       |                |               |                |
| subjects affected / exposed                    | 0 / 8 (0.00%)  | 0 / 3 (0.00%) | 0 / 2 (0.00%)  |
| occurrences (all)                              | 0              | 0             | 0              |
| Post procedural haematoma                      |                |               |                |
| subjects affected / exposed                    | 0 / 8 (0.00%)  | 0 / 3 (0.00%) | 0 / 2 (0.00%)  |
| occurrences (all)                              | 0              | 0             | 0              |
| Skin abrasion                                  |                |               |                |

|                                  |               |               |               |
|----------------------------------|---------------|---------------|---------------|
| subjects affected / exposed      | 0 / 8 (0.00%) | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all)                | 0             | 0             | 0             |
| Procedural pain                  |               |               |               |
| subjects affected / exposed      | 0 / 8 (0.00%) | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all)                | 0             | 0             | 0             |
| Subcutaneous haematoma           |               |               |               |
| subjects affected / exposed      | 0 / 8 (0.00%) | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all)                | 0             | 0             | 0             |
| Skin laceration                  |               |               |               |
| subjects affected / exposed      | 0 / 8 (0.00%) | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all)                | 0             | 0             | 0             |
| Tongue injury                    |               |               |               |
| subjects affected / exposed      | 0 / 8 (0.00%) | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all)                | 0             | 0             | 0             |
| Tooth fracture                   |               |               |               |
| subjects affected / exposed      | 0 / 8 (0.00%) | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all)                | 0             | 0             | 0             |
| Urinary tract stoma complication |               |               |               |
| subjects affected / exposed      | 0 / 8 (0.00%) | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all)                | 0             | 0             | 0             |
| Cardiac disorders                |               |               |               |
| Atrial fibrillation              |               |               |               |
| subjects affected / exposed      | 0 / 8 (0.00%) | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all)                | 0             | 0             | 0             |
| Angina pectoris                  |               |               |               |
| subjects affected / exposed      | 0 / 8 (0.00%) | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all)                | 0             | 0             | 0             |
| Palpitations                     |               |               |               |
| subjects affected / exposed      | 0 / 8 (0.00%) | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all)                | 0             | 0             | 0             |
| Tachycardia                      |               |               |               |
| subjects affected / exposed      | 0 / 8 (0.00%) | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all)                | 0             | 0             | 0             |
| Sinus tachycardia                |               |               |               |
| subjects affected / exposed      | 0 / 8 (0.00%) | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all)                | 0             | 0             | 0             |

|  |                     |                    |                     |
|--|---------------------|--------------------|---------------------|
| Ventricular arrhythmia<br>subjects affected / exposed<br>occurrences (all)   | 0 / 8 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0 | 0 / 2 (0.00%)<br>0  |
| Nervous system disorders   |                     |                    |                     |
| Ageusia<br>subjects affected / exposed<br>occurrences (all)                  | 0 / 8 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0 | 0 / 2 (0.00%)<br>0  |
| Agnosia<br>subjects affected / exposed<br>occurrences (all)                  | 0 / 8 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0 | 0 / 2 (0.00%)<br>0  |
| Amnesia<br>subjects affected / exposed<br>occurrences (all)                  | 0 / 8 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0 | 0 / 2 (0.00%)<br>0  |
| Cauda equina syndrome<br>subjects affected / exposed<br>occurrences (all)    | 0 / 8 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0 | 0 / 2 (0.00%)<br>0  |
| Disturbance in attention<br>subjects affected / exposed<br>occurrences (all) | 0 / 8 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0 | 0 / 2 (0.00%)<br>0  |
| Dizziness<br>subjects affected / exposed<br>occurrences (all)                | 0 / 8 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0 | 0 / 2 (0.00%)<br>0  |
| Dizziness postural<br>subjects affected / exposed<br>occurrences (all)       | 0 / 8 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0 | 0 / 2 (0.00%)<br>0  |
| Headache<br>subjects affected / exposed<br>occurrences (all)                 | 1 / 8 (12.50%)<br>1 | 0 / 3 (0.00%)<br>0 | 0 / 2 (0.00%)<br>0  |
| Dysgeusia<br>subjects affected / exposed<br>occurrences (all)                | 1 / 8 (12.50%)<br>1 | 0 / 3 (0.00%)<br>0 | 1 / 2 (50.00%)<br>2 |
| Motor dysfunction<br>subjects affected / exposed<br>occurrences (all)        | 1 / 8 (12.50%)<br>2 | 0 / 3 (0.00%)<br>0 | 0 / 2 (0.00%)<br>0  |
| Neuropathy peripheral  |                     |                    |                     |

|                                      |                |                |                |
|--------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed          | 0 / 8 (0.00%)  | 0 / 3 (0.00%)  | 1 / 2 (50.00%) |
| occurrences (all)                    | 0              | 0              | 2              |
| Peripheral sensory neuropathy        |                |                |                |
| subjects affected / exposed          | 0 / 8 (0.00%)  | 0 / 3 (0.00%)  | 0 / 2 (0.00%)  |
| occurrences (all)                    | 0              | 0              | 0              |
| Paraesthesia                         |                |                |                |
| subjects affected / exposed          | 0 / 8 (0.00%)  | 0 / 3 (0.00%)  | 0 / 2 (0.00%)  |
| occurrences (all)                    | 0              | 0              | 0              |
| Presyncope                           |                |                |                |
| subjects affected / exposed          | 0 / 8 (0.00%)  | 0 / 3 (0.00%)  | 0 / 2 (0.00%)  |
| occurrences (all)                    | 0              | 0              | 0              |
| Radiculopathy                        |                |                |                |
| subjects affected / exposed          | 0 / 8 (0.00%)  | 0 / 3 (0.00%)  | 0 / 2 (0.00%)  |
| occurrences (all)                    | 0              | 0              | 0              |
| Syncope                              |                |                |                |
| subjects affected / exposed          | 0 / 8 (0.00%)  | 0 / 3 (0.00%)  | 0 / 2 (0.00%)  |
| occurrences (all)                    | 0              | 0              | 0              |
| Somnolence                           |                |                |                |
| subjects affected / exposed          | 0 / 8 (0.00%)  | 0 / 3 (0.00%)  | 0 / 2 (0.00%)  |
| occurrences (all)                    | 0              | 0              | 0              |
| Sciatica                             |                |                |                |
| subjects affected / exposed          | 0 / 8 (0.00%)  | 0 / 3 (0.00%)  | 0 / 2 (0.00%)  |
| occurrences (all)                    | 0              | 0              | 0              |
| Taste disorder                       |                |                |                |
| subjects affected / exposed          | 0 / 8 (0.00%)  | 0 / 3 (0.00%)  | 0 / 2 (0.00%)  |
| occurrences (all)                    | 0              | 0              | 0              |
| Blood and lymphatic system disorders |                |                |                |
| Anaemia                              |                |                |                |
| subjects affected / exposed          | 1 / 8 (12.50%) | 1 / 3 (33.33%) | 1 / 2 (50.00%) |
| occurrences (all)                    | 1              | 1              | 3              |
| Coagulopathy                         |                |                |                |
| subjects affected / exposed          | 0 / 8 (0.00%)  | 0 / 3 (0.00%)  | 0 / 2 (0.00%)  |
| occurrences (all)                    | 0              | 0              | 0              |
| Eosinophilia                         |                |                |                |
| subjects affected / exposed          | 1 / 8 (12.50%) | 0 / 3 (0.00%)  | 0 / 2 (0.00%)  |
| occurrences (all)                    | 1              | 0              | 0              |

|  |                     |                     |                      |
|--|---------------------|---------------------|----------------------|
| Lymph node haemorrhage<br>subjects affected / exposed<br>occurrences (all)   | 1 / 8 (12.50%)<br>1 | 0 / 3 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0   |
| Lymph node pain<br>subjects affected / exposed<br>occurrences (all)          | 1 / 8 (12.50%)<br>1 | 0 / 3 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0   |
| Lymphadenopathy<br>subjects affected / exposed<br>occurrences (all)          | 1 / 8 (12.50%)<br>2 | 0 / 3 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0   |
| Neutropenia<br>subjects affected / exposed<br>occurrences (all)              | 3 / 8 (37.50%)<br>3 | 0 / 3 (0.00%)<br>0  | 2 / 2 (100.00%)<br>3 |
| Lymphopenia<br>subjects affected / exposed<br>occurrences (all)              | 0 / 8 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0   |
| Thrombocytopenia<br>subjects affected / exposed<br>occurrences (all)         | 4 / 8 (50.00%)<br>4 | 2 / 3 (66.67%)<br>2 | 1 / 2 (50.00%)<br>2  |
| Ear and labyrinth disorders  |                     |                     |                      |
| Ear congestion<br>subjects affected / exposed<br>occurrences (all)           | 0 / 8 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0   |
| Ear haemorrhage<br>subjects affected / exposed<br>occurrences (all)          | 0 / 8 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0   |
| Ear pain<br>subjects affected / exposed<br>occurrences (all)                 | 0 / 8 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0   |
| Vertigo<br>subjects affected / exposed<br>occurrences (all)                  | 0 / 8 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0  | 1 / 2 (50.00%)<br>1  |
| Eye disorders  |                     |                     |                      |
| Conjunctival haemorrhage<br>subjects affected / exposed<br>occurrences (all) | 0 / 8 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0   |
| Dry eye  |                     |                     |                      |

|                             |                |               |               |
|-----------------------------|----------------|---------------|---------------|
| subjects affected / exposed | 0 / 8 (0.00%)  | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all)           | 0              | 0             | 0             |
| Vitreous haemorrhage        |                |               |               |
| subjects affected / exposed | 0 / 8 (0.00%)  | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all)           | 0              | 0             | 0             |
| Vision blurred              |                |               |               |
| subjects affected / exposed | 0 / 8 (0.00%)  | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all)           | 0              | 0             | 0             |
| Periorbital oedema          |                |               |               |
| subjects affected / exposed | 0 / 8 (0.00%)  | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all)           | 0              | 0             | 0             |
| Gastrointestinal disorders  |                |               |               |
| Abdominal pain upper        |                |               |               |
| subjects affected / exposed | 0 / 8 (0.00%)  | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all)           | 0              | 0             | 0             |
| Abdominal pain              |                |               |               |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all)           | 2              | 0             | 0             |
| Abdominal distension        |                |               |               |
| subjects affected / exposed | 0 / 8 (0.00%)  | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all)           | 0              | 0             | 0             |
| Anal fissure                |                |               |               |
| subjects affected / exposed | 0 / 8 (0.00%)  | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all)           | 0              | 0             | 0             |
| Anal haemorrhage            |                |               |               |
| subjects affected / exposed | 0 / 8 (0.00%)  | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all)           | 0              | 0             | 0             |
| Aphthous ulcer              |                |               |               |
| subjects affected / exposed | 0 / 8 (0.00%)  | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all)           | 0              | 0             | 0             |
| Angular cheilitis           |                |               |               |
| subjects affected / exposed | 0 / 8 (0.00%)  | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all)           | 0              | 0             | 0             |
| Anal inflammation           |                |               |               |
| subjects affected / exposed | 0 / 8 (0.00%)  | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all)           | 0              | 0             | 0             |

|                                  |                |                |                 |
|----------------------------------|----------------|----------------|-----------------|
| Ascites                          |                |                |                 |
| subjects affected / exposed      | 0 / 8 (0.00%)  | 0 / 3 (0.00%)  | 0 / 2 (0.00%)   |
| occurrences (all)                | 0              | 0              | 0               |
| Constipation                     |                |                |                 |
| subjects affected / exposed      | 2 / 8 (25.00%) | 0 / 3 (0.00%)  | 0 / 2 (0.00%)   |
| occurrences (all)                | 2              | 0              | 0               |
| Diarrhoea                        |                |                |                 |
| subjects affected / exposed      | 2 / 8 (25.00%) | 0 / 3 (0.00%)  | 2 / 2 (100.00%) |
| occurrences (all)                | 3              | 0              | 5               |
| Dry mouth                        |                |                |                 |
| subjects affected / exposed      | 0 / 8 (0.00%)  | 0 / 3 (0.00%)  | 1 / 2 (50.00%)  |
| occurrences (all)                | 0              | 0              | 1               |
| Dyspepsia                        |                |                |                 |
| subjects affected / exposed      | 0 / 8 (0.00%)  | 0 / 3 (0.00%)  | 0 / 2 (0.00%)   |
| occurrences (all)                | 0              | 0              | 0               |
| Dysphagia                        |                |                |                 |
| subjects affected / exposed      | 0 / 8 (0.00%)  | 1 / 3 (33.33%) | 0 / 2 (0.00%)   |
| occurrences (all)                | 0              | 1              | 0               |
| Flatulence                       |                |                |                 |
| subjects affected / exposed      | 0 / 8 (0.00%)  | 0 / 3 (0.00%)  | 0 / 2 (0.00%)   |
| occurrences (all)                | 0              | 0              | 0               |
| Gastritis                        |                |                |                 |
| subjects affected / exposed      | 0 / 8 (0.00%)  | 0 / 3 (0.00%)  | 0 / 2 (0.00%)   |
| occurrences (all)                | 0              | 0              | 0               |
| Gastritis erosive                |                |                |                 |
| subjects affected / exposed      | 0 / 8 (0.00%)  | 0 / 3 (0.00%)  | 0 / 2 (0.00%)   |
| occurrences (all)                | 0              | 0              | 0               |
| Gastrointestinal disorder        |                |                |                 |
| subjects affected / exposed      | 0 / 8 (0.00%)  | 0 / 3 (0.00%)  | 0 / 2 (0.00%)   |
| occurrences (all)                | 0              | 0              | 0               |
| Gastrooesophageal reflux disease |                |                |                 |
| subjects affected / exposed      | 0 / 8 (0.00%)  | 0 / 3 (0.00%)  | 0 / 2 (0.00%)   |
| occurrences (all)                | 0              | 0              | 0               |
| Haemorrhoids                     |                |                |                 |
| subjects affected / exposed      | 0 / 8 (0.00%)  | 0 / 3 (0.00%)  | 0 / 2 (0.00%)   |
| occurrences (all)                | 0              | 0              | 0               |



|                                    |                |                |               |
|------------------------------------|----------------|----------------|---------------|
| Lip dry                            |                |                |               |
| subjects affected / exposed        | 0 / 8 (0.00%)  | 0 / 3 (0.00%)  | 0 / 2 (0.00%) |
| occurrences (all)                  | 0              | 0              | 0             |
| Melaena                            |                |                |               |
| subjects affected / exposed        | 0 / 8 (0.00%)  | 0 / 3 (0.00%)  | 0 / 2 (0.00%) |
| occurrences (all)                  | 0              | 0              | 0             |
| Lower gastrointestinal haemorrhage |                |                |               |
| subjects affected / exposed        | 0 / 8 (0.00%)  | 0 / 3 (0.00%)  | 0 / 2 (0.00%) |
| occurrences (all)                  | 0              | 0              | 0             |
| Nausea                             |                |                |               |
| subjects affected / exposed        | 1 / 8 (12.50%) | 1 / 3 (33.33%) | 0 / 2 (0.00%) |
| occurrences (all)                  | 1              | 1              | 0             |
| Odynophagia                        |                |                |               |
| subjects affected / exposed        | 0 / 8 (0.00%)  | 1 / 3 (33.33%) | 0 / 2 (0.00%) |
| occurrences (all)                  | 0              | 1              | 0             |
| Oral mucosal erythema              |                |                |               |
| subjects affected / exposed        | 0 / 8 (0.00%)  | 0 / 3 (0.00%)  | 0 / 2 (0.00%) |
| occurrences (all)                  | 0              | 0              | 0             |
| Retching                           |                |                |               |
| subjects affected / exposed        | 0 / 8 (0.00%)  | 0 / 3 (0.00%)  | 0 / 2 (0.00%) |
| occurrences (all)                  | 0              | 0              | 0             |
| Stomatitis                         |                |                |               |
| subjects affected / exposed        | 0 / 8 (0.00%)  | 1 / 3 (33.33%) | 0 / 2 (0.00%) |
| occurrences (all)                  | 0              | 1              | 0             |
| Subileus                           |                |                |               |
| subjects affected / exposed        | 0 / 8 (0.00%)  | 0 / 3 (0.00%)  | 0 / 2 (0.00%) |
| occurrences (all)                  | 0              | 0              | 0             |
| Toothache                          |                |                |               |
| subjects affected / exposed        | 0 / 8 (0.00%)  | 0 / 3 (0.00%)  | 0 / 2 (0.00%) |
| occurrences (all)                  | 0              | 0              | 0             |
| Vomiting                           |                |                |               |
| subjects affected / exposed        | 1 / 8 (12.50%) | 1 / 3 (33.33%) | 0 / 2 (0.00%) |
| occurrences (all)                  | 1              | 2              | 0             |
| Hepatobiliary disorders            |                |                |               |
| Cholangitis                        |                |                |               |

|  |                |                |                 |
|--|----------------|----------------|-----------------|
| subjects affected / exposed            | 0 / 8 (0.00%)  | 0 / 3 (0.00%)  | 0 / 2 (0.00%)   |
| occurrences (all)                      | 0              | 0              | 0               |
| Hepatic cytolysis                      |                |                |                 |
| subjects affected / exposed            | 0 / 8 (0.00%)  | 1 / 3 (33.33%) | 0 / 2 (0.00%)   |
| occurrences (all)                      | 0              | 1              | 0               |
| Hepatic pain                           |                |                |                 |
| subjects affected / exposed            | 0 / 8 (0.00%)  | 0 / 3 (0.00%)  | 0 / 2 (0.00%)   |
| occurrences (all)                      | 0              | 0              | 0               |
| Skin and subcutaneous tissue disorders |                |                |                 |
| Dermatitis psoriasiform                |                |                |                 |
| subjects affected / exposed            | 0 / 8 (0.00%)  | 0 / 3 (0.00%)  | 0 / 2 (0.00%)   |
| occurrences (all)                      | 0              | 0              | 0               |
| Dermatitis acneiform                   |                |                |                 |
| subjects affected / exposed            | 0 / 8 (0.00%)  | 0 / 3 (0.00%)  | 0 / 2 (0.00%)   |
| occurrences (all)                      | 0              | 0              | 0               |
| Dry skin                               |                |                |                 |
| subjects affected / exposed            | 1 / 8 (12.50%) | 0 / 3 (0.00%)  | 2 / 2 (100.00%) |
| occurrences (all)                      | 1              | 0              | 2               |
| Intertrigo                             |                |                |                 |
| subjects affected / exposed            | 0 / 8 (0.00%)  | 0 / 3 (0.00%)  | 0 / 2 (0.00%)   |
| occurrences (all)                      | 0              | 0              | 0               |
| Macule                                 |                |                |                 |
| subjects affected / exposed            | 0 / 8 (0.00%)  | 0 / 3 (0.00%)  | 0 / 2 (0.00%)   |
| occurrences (all)                      | 0              | 0              | 0               |
| Night sweats                           |                |                |                 |
| subjects affected / exposed            | 1 / 8 (12.50%) | 0 / 3 (0.00%)  | 0 / 2 (0.00%)   |
| occurrences (all)                      | 1              | 0              | 0               |
| Eczema                                 |                |                |                 |
| subjects affected / exposed            | 0 / 8 (0.00%)  | 0 / 3 (0.00%)  | 0 / 2 (0.00%)   |
| occurrences (all)                      | 0              | 0              | 0               |
| Erythema                               |                |                |                 |
| subjects affected / exposed            | 0 / 8 (0.00%)  | 0 / 3 (0.00%)  | 1 / 2 (50.00%)  |
| occurrences (all)                      | 0              | 0              | 1               |
| Prurigo                                |                |                |                 |
| subjects affected / exposed            | 0 / 8 (0.00%)  | 0 / 3 (0.00%)  | 0 / 2 (0.00%)   |
| occurrences (all)                      | 0              | 0              | 0               |

|                             |                |                |                |
|-----------------------------|----------------|----------------|----------------|
| Pruritus                    |                |                |                |
| subjects affected / exposed | 0 / 8 (0.00%)  | 0 / 3 (0.00%)  | 0 / 2 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0              |
| Psoriasis                   |                |                |                |
| subjects affected / exposed | 0 / 8 (0.00%)  | 0 / 3 (0.00%)  | 0 / 2 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0              |
| Petechiae                   |                |                |                |
| subjects affected / exposed | 0 / 8 (0.00%)  | 0 / 3 (0.00%)  | 0 / 2 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0              |
| Skin ulcer                  |                |                |                |
| subjects affected / exposed | 0 / 8 (0.00%)  | 0 / 3 (0.00%)  | 0 / 2 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0              |
| Rash                        |                |                |                |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 3 (0.00%)  | 0 / 2 (0.00%)  |
| occurrences (all)           | 1              | 0              | 0              |
| Rash maculo-papular         |                |                |                |
| subjects affected / exposed | 0 / 8 (0.00%)  | 1 / 3 (33.33%) | 0 / 2 (0.00%)  |
| occurrences (all)           | 0              | 1              | 0              |
| Purpura                     |                |                |                |
| subjects affected / exposed | 0 / 8 (0.00%)  | 0 / 3 (0.00%)  | 0 / 2 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0              |
| Urticaria                   |                |                |                |
| subjects affected / exposed | 0 / 8 (0.00%)  | 0 / 3 (0.00%)  | 0 / 2 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0              |
| Renal and urinary disorders |                |                |                |
| Dysuria                     |                |                |                |
| subjects affected / exposed | 0 / 8 (0.00%)  | 0 / 3 (0.00%)  | 0 / 2 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0              |
| Haematuria                  |                |                |                |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 3 (0.00%)  | 0 / 2 (0.00%)  |
| occurrences (all)           | 1              | 0              | 0              |
| Pollakiuria                 |                |                |                |
| subjects affected / exposed | 0 / 8 (0.00%)  | 0 / 3 (0.00%)  | 1 / 2 (50.00%) |
| occurrences (all)           | 0              | 0              | 1              |
| Urinary tract pain          |                |                |                |

|   |                |               |                |
|---|----------------|---------------|----------------|
| subjects affected / exposed                     | 0 / 8 (0.00%)  | 0 / 3 (0.00%) | 0 / 2 (0.00%)  |
| occurrences (all)                               | 0              | 0             | 0              |
| Urinary retention                               |                |               |                |
| subjects affected / exposed                     | 0 / 8 (0.00%)  | 0 / 3 (0.00%) | 0 / 2 (0.00%)  |
| occurrences (all)                               | 0              | 0             | 0              |
| Renal failure                                   |                |               |                |
| subjects affected / exposed                     | 1 / 8 (12.50%) | 0 / 3 (0.00%) | 0 / 2 (0.00%)  |
| occurrences (all)                               | 1              | 0             | 0              |
| Endocrine disorders                             |                |               |                |
| Hyperthyroidism                                 |                |               |                |
| subjects affected / exposed                     | 0 / 8 (0.00%)  | 0 / 3 (0.00%) | 0 / 2 (0.00%)  |
| occurrences (all)                               | 0              | 0             | 0              |
| Musculoskeletal and connective tissue disorders |                |               |                |
| Arthralgia                                      |                |               |                |
| subjects affected / exposed                     | 0 / 8 (0.00%)  | 0 / 3 (0.00%) | 0 / 2 (0.00%)  |
| occurrences (all)                               | 0              | 0             | 0              |
| Back pain                                       |                |               |                |
| subjects affected / exposed                     | 0 / 8 (0.00%)  | 0 / 3 (0.00%) | 1 / 2 (50.00%) |
| occurrences (all)                               | 0              | 0             | 1              |
| Bone pain                                       |                |               |                |
| subjects affected / exposed                     | 0 / 8 (0.00%)  | 0 / 3 (0.00%) | 0 / 2 (0.00%)  |
| occurrences (all)                               | 0              | 0             | 0              |
| Flank pain                                      |                |               |                |
| subjects affected / exposed                     | 0 / 8 (0.00%)  | 0 / 3 (0.00%) | 0 / 2 (0.00%)  |
| occurrences (all)                               | 0              | 0             | 0              |
| Groin pain                                      |                |               |                |
| subjects affected / exposed                     | 0 / 8 (0.00%)  | 0 / 3 (0.00%) | 0 / 2 (0.00%)  |
| occurrences (all)                               | 0              | 0             | 0              |
| Muscular weakness                               |                |               |                |
| subjects affected / exposed                     | 0 / 8 (0.00%)  | 0 / 3 (0.00%) | 0 / 2 (0.00%)  |
| occurrences (all)                               | 0              | 0             | 0              |
| Muscle spasms                                   |                |               |                |
| subjects affected / exposed                     | 1 / 8 (12.50%) | 0 / 3 (0.00%) | 1 / 2 (50.00%) |
| occurrences (all)                               | 2              | 0             | 1              |
| Myalgia   |                |               |                |

|   |                     |                    |                    |
|---|---------------------|--------------------|--------------------|
| subjects affected / exposed<br>occurrences (all)                                  | 0 / 8 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0 | 0 / 2 (0.00%)<br>0 |
| Neck pain<br>subjects affected / exposed<br>occurrences (all)                     | 0 / 8 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0 | 0 / 2 (0.00%)<br>0 |
| Pain in extremity<br>subjects affected / exposed<br>occurrences (all)             | 2 / 8 (25.00%)<br>2 | 0 / 3 (0.00%)<br>0 | 0 / 2 (0.00%)<br>0 |
| Pubic pain<br>subjects affected / exposed<br>occurrences (all)                    | 0 / 8 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0 | 0 / 2 (0.00%)<br>0 |
| Infections and infestations   |                     |                    |                    |
| Bronchitis<br>subjects affected / exposed<br>occurrences (all)                    | 1 / 8 (12.50%)<br>1 | 0 / 3 (0.00%)<br>0 | 0 / 2 (0.00%)<br>0 |
| Bronchitis viral<br>subjects affected / exposed<br>occurrences (all)              | 0 / 8 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0 | 0 / 2 (0.00%)<br>0 |
| Clostridial infection<br>subjects affected / exposed<br>occurrences (all)         | 0 / 8 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0 | 0 / 2 (0.00%)<br>0 |
| Clostridium difficile colitis<br>subjects affected / exposed<br>occurrences (all) | 0 / 8 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0 | 0 / 2 (0.00%)<br>0 |
| Conjunctivitis<br>subjects affected / exposed<br>occurrences (all)                | 0 / 8 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0 | 0 / 2 (0.00%)<br>0 |
| Erysipelas<br>subjects affected / exposed<br>occurrences (all)                    | 0 / 8 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0 | 0 / 2 (0.00%)<br>0 |
| Diverticulitis<br>subjects affected / exposed<br>occurrences (all)                | 0 / 8 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0 | 0 / 2 (0.00%)<br>0 |
| Cystitis<br>subjects affected / exposed<br>occurrences (all)                      | 0 / 8 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0 | 0 / 2 (0.00%)<br>0 |

|                                     |                |               |               |
|-------------------------------------|----------------|---------------|---------------|
| Gastroenteritis                     |                |               |               |
| subjects affected / exposed         | 0 / 8 (0.00%)  | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all)                   | 0              | 0             | 0             |
| Folliculitis                        |                |               |               |
| subjects affected / exposed         | 0 / 8 (0.00%)  | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all)                   | 0              | 0             | 0             |
| Escherichia urinary tract infection |                |               |               |
| subjects affected / exposed         | 0 / 8 (0.00%)  | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all)                   | 0              | 0             | 0             |
| Genital herpes simplex              |                |               |               |
| subjects affected / exposed         | 0 / 8 (0.00%)  | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all)                   | 0              | 0             | 0             |
| Genital infection fungal            |                |               |               |
| subjects affected / exposed         | 0 / 8 (0.00%)  | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all)                   | 0              | 0             | 0             |
| Herpes dermatitis                   |                |               |               |
| subjects affected / exposed         | 0 / 8 (0.00%)  | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all)                   | 0              | 0             | 0             |
| Impetigo                            |                |               |               |
| subjects affected / exposed         | 0 / 8 (0.00%)  | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all)                   | 0              | 0             | 0             |
| Herpes zoster                       |                |               |               |
| subjects affected / exposed         | 0 / 8 (0.00%)  | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all)                   | 0              | 0             | 0             |
| Influenza                           |                |               |               |
| subjects affected / exposed         | 1 / 8 (12.50%) | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all)                   | 1              | 0             | 0             |
| Infection                           |                |               |               |
| subjects affected / exposed         | 0 / 8 (0.00%)  | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all)                   | 0              | 0             | 0             |
| Nasopharyngitis                     |                |               |               |
| subjects affected / exposed         | 0 / 8 (0.00%)  | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all)                   | 0              | 0             | 0             |
| Oesophageal infection               |                |               |               |
| subjects affected / exposed         | 0 / 8 (0.00%)  | 0 / 3 (0.00%) | 0 / 2 (0.00%) |
| occurrences (all)                   | 0              | 0             | 0             |

|                                       |               |               |                |
|---------------------------------------|---------------|---------------|----------------|
| Pharyngitis                           |               |               |                |
| subjects affected / exposed           | 0 / 8 (0.00%) | 0 / 3 (0.00%) | 0 / 2 (0.00%)  |
| occurrences (all)                     | 0             | 0             | 0              |
| Oral herpes                           |               |               |                |
| subjects affected / exposed           | 0 / 8 (0.00%) | 0 / 3 (0.00%) | 0 / 2 (0.00%)  |
| occurrences (all)                     | 0             | 0             | 0              |
| Pneumonia                             |               |               |                |
| subjects affected / exposed           | 0 / 8 (0.00%) | 0 / 3 (0.00%) | 0 / 2 (0.00%)  |
| occurrences (all)                     | 0             | 0             | 0              |
| Rash pustular                         |               |               |                |
| subjects affected / exposed           | 0 / 8 (0.00%) | 0 / 3 (0.00%) | 0 / 2 (0.00%)  |
| occurrences (all)                     | 0             | 0             | 0              |
| Respiratory tract infection           |               |               |                |
| subjects affected / exposed           | 0 / 8 (0.00%) | 0 / 3 (0.00%) | 0 / 2 (0.00%)  |
| occurrences (all)                     | 0             | 0             | 0              |
| Respiratory tract infection bacterial |               |               |                |
| subjects affected / exposed           | 0 / 8 (0.00%) | 0 / 3 (0.00%) | 0 / 2 (0.00%)  |
| occurrences (all)                     | 0             | 0             | 0              |
| Sinusitis                             |               |               |                |
| subjects affected / exposed           | 0 / 8 (0.00%) | 0 / 3 (0.00%) | 0 / 2 (0.00%)  |
| occurrences (all)                     | 0             | 0             | 0              |
| Tooth abscess                         |               |               |                |
| subjects affected / exposed           | 0 / 8 (0.00%) | 0 / 3 (0.00%) | 0 / 2 (0.00%)  |
| occurrences (all)                     | 0             | 0             | 0              |
| Tooth infection                       |               |               |                |
| subjects affected / exposed           | 0 / 8 (0.00%) | 0 / 3 (0.00%) | 0 / 2 (0.00%)  |
| occurrences (all)                     | 0             | 0             | 0              |
| Tracheitis                            |               |               |                |
| subjects affected / exposed           | 0 / 8 (0.00%) | 0 / 3 (0.00%) | 0 / 2 (0.00%)  |
| occurrences (all)                     | 0             | 0             | 0              |
| Upper respiratory tract infection     |               |               |                |
| subjects affected / exposed           | 0 / 8 (0.00%) | 0 / 3 (0.00%) | 0 / 2 (0.00%)  |
| occurrences (all)                     | 0             | 0             | 0              |
| Urinary tract infection enterococcal  |               |               |                |
| subjects affected / exposed           | 0 / 8 (0.00%) | 0 / 3 (0.00%) | 1 / 2 (50.00%) |
| occurrences (all)                     | 0             | 0             | 1              |

|                                    |                |                |               |
|------------------------------------|----------------|----------------|---------------|
| Urinary tract infection            |                |                |               |
| subjects affected / exposed        | 0 / 8 (0.00%)  | 0 / 3 (0.00%)  | 0 / 2 (0.00%) |
| occurrences (all)                  | 0              | 0              | 0             |
| Mucosal infection                  |                |                |               |
| subjects affected / exposed        | 0 / 8 (0.00%)  | 0 / 3 (0.00%)  | 0 / 2 (0.00%) |
| occurrences (all)                  | 0              | 0              | 0             |
| Stoma site infection               |                |                |               |
| subjects affected / exposed        | 0 / 8 (0.00%)  | 0 / 3 (0.00%)  | 0 / 2 (0.00%) |
| occurrences (all)                  | 0              | 0              | 0             |
| Metabolism and nutrition disorders |                |                |               |
| Acidosis                           |                |                |               |
| subjects affected / exposed        | 0 / 8 (0.00%)  | 0 / 3 (0.00%)  | 0 / 2 (0.00%) |
| occurrences (all)                  | 0              | 0              | 0             |
| Decreased appetite                 |                |                |               |
| subjects affected / exposed        | 1 / 8 (12.50%) | 1 / 3 (33.33%) | 0 / 2 (0.00%) |
| occurrences (all)                  | 1              | 2              | 0             |
| Cell death                         |                |                |               |
| subjects affected / exposed        | 0 / 8 (0.00%)  | 0 / 3 (0.00%)  | 0 / 2 (0.00%) |
| occurrences (all)                  | 0              | 0              | 0             |
| Dehydration                        |                |                |               |
| subjects affected / exposed        | 0 / 8 (0.00%)  | 0 / 3 (0.00%)  | 0 / 2 (0.00%) |
| occurrences (all)                  | 0              | 0              | 0             |
| Fluid retention                    |                |                |               |
| subjects affected / exposed        | 1 / 8 (12.50%) | 0 / 3 (0.00%)  | 0 / 2 (0.00%) |
| occurrences (all)                  | 1              | 0              | 0             |
| Folate deficiency                  |                |                |               |
| subjects affected / exposed        | 0 / 8 (0.00%)  | 0 / 3 (0.00%)  | 0 / 2 (0.00%) |
| occurrences (all)                  | 0              | 0              | 0             |
| Gout                               |                |                |               |
| subjects affected / exposed        | 0 / 8 (0.00%)  | 0 / 3 (0.00%)  | 0 / 2 (0.00%) |
| occurrences (all)                  | 0              | 0              | 0             |
| Hypercalcaemia                     |                |                |               |
| subjects affected / exposed        | 0 / 8 (0.00%)  | 0 / 3 (0.00%)  | 0 / 2 (0.00%) |
| occurrences (all)                  | 0              | 0              | 0             |
| Hyperkalaemia                      |                |                |               |



|                             |               |                |               |
|-----------------------------|---------------|----------------|---------------|
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 3 (0.00%)  | 0 / 2 (0.00%) |
| occurrences (all)           | 0             | 0              | 0             |
| Hyperglycaemia              |               |                |               |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 3 (0.00%)  | 0 / 2 (0.00%) |
| occurrences (all)           | 0             | 0              | 0             |
| Hyperphosphataemia          |               |                |               |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 3 (0.00%)  | 0 / 2 (0.00%) |
| occurrences (all)           | 0             | 0              | 0             |
| Hypoalbuminaemia            |               |                |               |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 3 (0.00%)  | 0 / 2 (0.00%) |
| occurrences (all)           | 0             | 0              | 0             |
| Hypocalcaemia               |               |                |               |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 3 (0.00%)  | 0 / 2 (0.00%) |
| occurrences (all)           | 0             | 0              | 0             |
| Hypokalaemia                |               |                |               |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 3 (0.00%)  | 0 / 2 (0.00%) |
| occurrences (all)           | 0             | 0              | 0             |
| Hypomagnesaemia             |               |                |               |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 3 (0.00%)  | 0 / 2 (0.00%) |
| occurrences (all)           | 0             | 0              | 0             |
| Hyponatraemia               |               |                |               |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 3 (33.33%) | 0 / 2 (0.00%) |
| occurrences (all)           | 0             | 2              | 0             |
| Hypophosphataemia           |               |                |               |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 3 (33.33%) | 0 / 2 (0.00%) |
| occurrences (all)           | 0             | 2              | 0             |
| Malnutrition                |               |                |               |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 3 (0.00%)  | 0 / 2 (0.00%) |
| occurrences (all)           | 0             | 0              | 0             |

| <b>Non-serious adverse events</b>                                   | Phase Ia - Schedule C: 4/2 mg BI 894999 (DLBCL patients) | Phase Ia - Schedule B: 2.5 mg BI 894999 (DLBCL patients) | Phase Ia - Schedule B: 2.5 mg BI 894999 (DLBCL patients) |
|---|--|--|--|
| Total subjects affected by non-serious adverse events               |  |  |  |
| subjects affected / exposed   | 2 / 2 (100.00%)  | 2 / 2 (100.00%)  | 4 / 4 (100.00%)  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |  |  |  |

|   |                     |                      |                     |
|---|---------------------|----------------------|---------------------|
| Tumour pain<br>subjects affected / exposed<br>occurrences (all)             | 0 / 2 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0   | 0 / 4 (0.00%)<br>0  |
| Vascular disorders  |                     |                      |                     |
| Hypotension<br>subjects affected / exposed<br>occurrences (all)             | 0 / 2 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0   | 0 / 4 (0.00%)<br>0  |
| Hypertension<br>subjects affected / exposed<br>occurrences (all)            | 0 / 2 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0   | 0 / 4 (0.00%)<br>0  |
| Haematoma<br>subjects affected / exposed<br>occurrences (all)               | 0 / 2 (0.00%)<br>0  | 2 / 2 (100.00%)<br>3 | 1 / 4 (25.00%)<br>1 |
| Orthostatic hypotension<br>subjects affected / exposed<br>occurrences (all) | 0 / 2 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0   | 0 / 4 (0.00%)<br>0  |
| Pallor<br>subjects affected / exposed<br>occurrences (all)                  | 0 / 2 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0   | 0 / 4 (0.00%)<br>0  |
| General disorders and administration<br>site conditions                     |                     |                      |                     |
| Chest discomfort<br>subjects affected / exposed<br>occurrences (all)        | 0 / 2 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0   | 0 / 4 (0.00%)<br>0  |
| Asthenia<br>subjects affected / exposed<br>occurrences (all)                | 0 / 2 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0   | 0 / 4 (0.00%)<br>0  |
| Chest pain<br>subjects affected / exposed<br>occurrences (all)              | 0 / 2 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0   | 0 / 4 (0.00%)<br>0  |
| Fatigue<br>subjects affected / exposed<br>occurrences (all)                 | 1 / 2 (50.00%)<br>1 | 1 / 2 (50.00%)<br>1  | 3 / 4 (75.00%)<br>5 |
| Facial pain<br>subjects affected / exposed<br>occurrences (all)             | 0 / 2 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0   | 0 / 4 (0.00%)<br>0  |
| Chills  |                     |                      |                     |

|                                       |                |                |               |
|---------------------------------------|----------------|----------------|---------------|
| subjects affected / exposed           | 0 / 2 (0.00%)  | 1 / 2 (50.00%) | 0 / 4 (0.00%) |
| occurrences (all)                     | 0              | 2              | 0             |
| Gait disturbance                      |                |                |               |
| subjects affected / exposed           | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)                     | 0              | 0              | 0             |
| General physical health deterioration |                |                |               |
| subjects affected / exposed           | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)                     | 0              | 0              | 0             |
| Generalised oedema                    |                |                |               |
| subjects affected / exposed           | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)                     | 0              | 0              | 0             |
| Malaise                               |                |                |               |
| subjects affected / exposed           | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)                     | 0              | 0              | 0             |
| Hypothermia                           |                |                |               |
| subjects affected / exposed           | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)                     | 0              | 0              | 0             |
| Oedema peripheral                     |                |                |               |
| subjects affected / exposed           | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)                     | 0              | 0              | 0             |
| Non-cardiac chest pain                |                |                |               |
| subjects affected / exposed           | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)                     | 0              | 0              | 0             |
| Pain                                  |                |                |               |
| subjects affected / exposed           | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)                     | 0              | 0              | 0             |
| Pyrexia                               |                |                |               |
| subjects affected / exposed           | 1 / 2 (50.00%) | 1 / 2 (50.00%) | 0 / 4 (0.00%) |
| occurrences (all)                     | 1              | 2              | 0             |
| Peripheral swelling                   |                |                |               |
| subjects affected / exposed           | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)                     | 0              | 0              | 0             |
| Immune system disorders               |                |                |               |
| Hypersensitivity                      |                |                |               |
| subjects affected / exposed           | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)                     | 0              | 0              | 0             |

|  |                     |                    |                    |
|--|---------------------|--------------------|--------------------|
| Iodine allergy<br>subjects affected / exposed<br>occurrences (all)           | 0 / 2 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0 | 0 / 4 (0.00%)<br>0 |
| Reproductive system and breast disorders                                     |                     |                    |                    |
| Erectile dysfunction<br>subjects affected / exposed<br>occurrences (all)     | 0 / 2 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0 | 0 / 4 (0.00%)<br>0 |
| Heavy menstrual bleeding<br>subjects affected / exposed<br>occurrences (all) | 0 / 2 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0 | 0 / 4 (0.00%)<br>0 |
| Oedema genital<br>subjects affected / exposed<br>occurrences (all)           | 0 / 2 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0 | 0 / 4 (0.00%)<br>0 |
| Perineal pain<br>subjects affected / exposed<br>occurrences (all)            | 0 / 2 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0 | 0 / 4 (0.00%)<br>0 |
| Scrotal oedema<br>subjects affected / exposed<br>occurrences (all)           | 0 / 2 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0 | 0 / 4 (0.00%)<br>0 |
| Testicular pain<br>subjects affected / exposed<br>occurrences (all)          | 0 / 2 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0 | 0 / 4 (0.00%)<br>0 |
| Vulvovaginal discomfort<br>subjects affected / exposed<br>occurrences (all)  | 0 / 2 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0 | 0 / 4 (0.00%)<br>0 |
| Vaginal haemorrhage<br>subjects affected / exposed<br>occurrences (all)      | 0 / 2 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0 | 0 / 4 (0.00%)<br>0 |
| Respiratory, thoracic and mediastinal disorders                              |                     |                    |                    |
| Atelectasis<br>subjects affected / exposed<br>occurrences (all)              | 0 / 2 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0 | 0 / 4 (0.00%)<br>0 |
| Dysphonia<br>subjects affected / exposed<br>occurrences (all)                | 1 / 2 (50.00%)<br>1 | 0 / 2 (0.00%)<br>0 | 0 / 4 (0.00%)<br>0 |
| Cough  |                     |                    |                    |

|                             |                |                |                |
|-----------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 2 (0.00%)  | 1 / 2 (50.00%) | 0 / 4 (0.00%)  |
| occurrences (all)           | 0              | 1              | 0              |
| Dyspnoea                    |                |                |                |
| subjects affected / exposed | 1 / 2 (50.00%) | 0 / 2 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)           | 1              | 0              | 0              |
| Dyspnoea exertional         |                |                |                |
| subjects affected / exposed | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0              |
| Epistaxis                   |                |                |                |
| subjects affected / exposed | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 2 / 4 (50.00%) |
| occurrences (all)           | 0              | 0              | 3              |
| Laryngeal inflammation      |                |                |                |
| subjects affected / exposed | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0              |
| Haemoptysis                 |                |                |                |
| subjects affected / exposed | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0              |
| Nasal discomfort            |                |                |                |
| subjects affected / exposed | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0              |
| Oropharyngeal pain          |                |                |                |
| subjects affected / exposed | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0              |
| Pharyngeal inflammation     |                |                |                |
| subjects affected / exposed | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0              |
| Pleural effusion            |                |                |                |
| subjects affected / exposed | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0              |
| Pleuritic pain              |                |                |                |
| subjects affected / exposed | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0              |
| Productive cough            |                |                |                |
| subjects affected / exposed | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0              |
| Rhinorrhoea                 |                |                |                |

|  |                     |                     |                    |
|--|---------------------|---------------------|--------------------|
| subjects affected / exposed<br>occurrences (all)                                 | 0 / 2 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0 |
| Respiratory tract congestion<br>subjects affected / exposed<br>occurrences (all) | 0 / 2 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0 |
| Wheezing<br>subjects affected / exposed<br>occurrences (all)                     | 0 / 2 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0 |
| Psychiatric disorders  |                     |                     |                    |
| Affective disorder<br>subjects affected / exposed<br>occurrences (all)           | 0 / 2 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0 |
| Agitation<br>subjects affected / exposed<br>occurrences (all)                    | 0 / 2 (0.00%)<br>0  | 1 / 2 (50.00%)<br>1 | 0 / 4 (0.00%)<br>0 |
| Anxiety<br>subjects affected / exposed<br>occurrences (all)                      | 0 / 2 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0 |
| Confusional state<br>subjects affected / exposed<br>occurrences (all)            | 0 / 2 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0 |
| Depression<br>subjects affected / exposed<br>occurrences (all)                   | 0 / 2 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0 |
| Insomnia<br>subjects affected / exposed<br>occurrences (all)                     | 1 / 2 (50.00%)<br>1 | 0 / 2 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0 |
| Hallucination<br>subjects affected / exposed<br>occurrences (all)                | 0 / 2 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0 |
| Personality change<br>subjects affected / exposed<br>occurrences (all)           | 0 / 2 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0 |
| Sleep disorder<br>subjects affected / exposed<br>occurrences (all)               | 0 / 2 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0 |

|   |               |                |               |
|---|---------------|----------------|---------------|
| Investigations                                  |               |                |               |
| Activated partial thromboplastin time prolonged |               |                |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 1 / 2 (50.00%) | 0 / 4 (0.00%) |
| occurrences (all)                               | 0             | 2              | 0             |
| Activated partial thromboplastin time shortened |               |                |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)                               | 0             | 0              | 0             |
| Alanine aminotransferase increased              |               |                |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)                               | 0             | 0              | 0             |
| Aspartate aminotransferase increased            |               |                |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)                               | 0             | 0              | 0             |
| Blood alkaline phosphatase increased            |               |                |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)                               | 0             | 0              | 0             |
| Blood antidiuretic hormone decreased            |               |                |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)                               | 0             | 0              | 0             |
| Blood bilirubin increased                       |               |                |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)                               | 0             | 0              | 0             |
| Blood creatine phosphokinase increased          |               |                |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)                               | 0             | 0              | 0             |
| Blood creatinine increased                      |               |                |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)                               | 0             | 0              | 0             |
| Blood magnesium decreased                       |               |                |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)                               | 0             | 0              | 0             |
| Blood glucose increased                         |               |                |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)                               | 0             | 0              | 0             |

|   |                    |                     |                    |
|---|--------------------|---------------------|--------------------|
| C-reactive protein increased<br>subjects affected / exposed<br>occurrences (all)                | 0 / 2 (0.00%)<br>0 | 0 / 2 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0 |
| Cardiac murmur<br>subjects affected / exposed<br>occurrences (all)                              | 0 / 2 (0.00%)<br>0 | 0 / 2 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0 |
| Cortisol increased<br>subjects affected / exposed<br>occurrences (all)                          | 0 / 2 (0.00%)<br>0 | 0 / 2 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0 |
| Echocardiogram abnormal<br>subjects affected / exposed<br>occurrences (all)                     | 0 / 2 (0.00%)<br>0 | 0 / 2 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0 |
| Electrocardiogram PR prolongation<br>subjects affected / exposed<br>occurrences (all)           | 0 / 2 (0.00%)<br>0 | 0 / 2 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0 |
| Ejection fraction decreased<br>subjects affected / exposed<br>occurrences (all)                 | 0 / 2 (0.00%)<br>0 | 0 / 2 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0 |
| Electrocardiogram ST segment<br>elevation<br>subjects affected / exposed<br>occurrences (all)   | 0 / 2 (0.00%)<br>0 | 0 / 2 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0 |
| Gamma-glutamyltransferase<br>increased<br>subjects affected / exposed<br>occurrences (all)      | 0 / 2 (0.00%)<br>0 | 0 / 2 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0 |
| Electrocardiogram T wave inversion<br>subjects affected / exposed<br>occurrences (all)          | 0 / 2 (0.00%)<br>0 | 0 / 2 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0 |
| International normalised ratio<br>increased<br>subjects affected / exposed<br>occurrences (all) | 0 / 2 (0.00%)<br>0 | 0 / 2 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0 |
| Lymphocyte count decreased<br>subjects affected / exposed<br>occurrences (all)                  | 0 / 2 (0.00%)<br>0 | 1 / 2 (50.00%)<br>3 | 0 / 4 (0.00%)<br>0 |
| Neutrophil count decreased  |                    |                     |                    |



|  |                |                |                |
|--|----------------|----------------|----------------|
| subjects affected / exposed                    | 0 / 2 (0.00%)  | 1 / 2 (50.00%) | 0 / 4 (0.00%)  |
| occurrences (all)                              | 0              | 8              | 0              |
| Platelet count decreased                       |                |                |                |
| subjects affected / exposed                    | 1 / 2 (50.00%) | 0 / 2 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                              | 2              | 0              | 0              |
| Prothrombin level decreased                    |                |                |                |
| subjects affected / exposed                    | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                              | 0              | 0              | 0              |
| Troponin I increased                           |                |                |                |
| subjects affected / exposed                    | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                              | 0              | 0              | 0              |
| Troponin T increased                           |                |                |                |
| subjects affected / exposed                    | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 1 / 4 (25.00%) |
| occurrences (all)                              | 0              | 0              | 1              |
| Troponin increased                             |                |                |                |
| subjects affected / exposed                    | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                              | 0              | 0              | 0              |
| Urine output decreased                         |                |                |                |
| subjects affected / exposed                    | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                              | 0              | 0              | 0              |
| Weight decreased                               |                |                |                |
| subjects affected / exposed                    | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                              | 0              | 0              | 0              |
| White blood cell count decreased               |                |                |                |
| subjects affected / exposed                    | 0 / 2 (0.00%)  | 1 / 2 (50.00%) | 0 / 4 (0.00%)  |
| occurrences (all)                              | 0              | 7              | 0              |
| Injury, poisoning and procedural complications |                |                |                |
| Contusion                                      |                |                |                |
| subjects affected / exposed                    | 0 / 2 (0.00%)  | 1 / 2 (50.00%) | 0 / 4 (0.00%)  |
| occurrences (all)                              | 0              | 1              | 0              |
| Face injury                                    |                |                |                |
| subjects affected / exposed                    | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                              | 0              | 0              | 0              |
| Infusion related reaction                      |                |                |                |

|                                  |                |                |               |
|----------------------------------|----------------|----------------|---------------|
| subjects affected / exposed      | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)                | 0              | 0              | 0             |
| Limb injury                      |                |                |               |
| subjects affected / exposed      | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)                | 0              | 0              | 0             |
| Muscle rupture                   |                |                |               |
| subjects affected / exposed      | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)                | 0              | 0              | 0             |
| Overdose                         |                |                |               |
| subjects affected / exposed      | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)                | 0              | 0              | 0             |
| Post procedural haematoma        |                |                |               |
| subjects affected / exposed      | 0 / 2 (0.00%)  | 1 / 2 (50.00%) | 0 / 4 (0.00%) |
| occurrences (all)                | 0              | 1              | 0             |
| Skin abrasion                    |                |                |               |
| subjects affected / exposed      | 0 / 2 (0.00%)  | 1 / 2 (50.00%) | 0 / 4 (0.00%) |
| occurrences (all)                | 0              | 1              | 0             |
| Procedural pain                  |                |                |               |
| subjects affected / exposed      | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)                | 0              | 0              | 0             |
| Subcutaneous haematoma           |                |                |               |
| subjects affected / exposed      | 1 / 2 (50.00%) | 0 / 2 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)                | 1              | 0              | 0             |
| Skin laceration                  |                |                |               |
| subjects affected / exposed      | 0 / 2 (0.00%)  | 1 / 2 (50.00%) | 0 / 4 (0.00%) |
| occurrences (all)                | 0              | 1              | 0             |
| Tongue injury                    |                |                |               |
| subjects affected / exposed      | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)                | 0              | 0              | 0             |
| Tooth fracture                   |                |                |               |
| subjects affected / exposed      | 0 / 2 (0.00%)  | 1 / 2 (50.00%) | 0 / 4 (0.00%) |
| occurrences (all)                | 0              | 1              | 0             |
| Urinary tract stoma complication |                |                |               |
| subjects affected / exposed      | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)                | 0              | 0              | 0             |
| Cardiac disorders                |                |                |               |

|                             |               |                |               |
|-----------------------------|---------------|----------------|---------------|
| Atrial fibrillation         |               |                |               |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)           | 0             | 0              | 0             |
| Angina pectoris             |               |                |               |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)           | 0             | 0              | 0             |
| Palpitations                |               |                |               |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)           | 0             | 0              | 0             |
| Tachycardia                 |               |                |               |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)           | 0             | 0              | 0             |
| Sinus tachycardia           |               |                |               |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)           | 0             | 0              | 0             |
| Ventricular arrhythmia      |               |                |               |
| subjects affected / exposed | 0 / 2 (0.00%) | 1 / 2 (50.00%) | 0 / 4 (0.00%) |
| occurrences (all)           | 0             | 1              | 0             |
| Nervous system disorders    |               |                |               |
| Ageusia                     |               |                |               |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)           | 0             | 0              | 0             |
| Agnosia                     |               |                |               |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)           | 0             | 0              | 0             |
| Amnesia                     |               |                |               |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)           | 0             | 0              | 0             |
| Cauda equina syndrome       |               |                |               |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)           | 0             | 0              | 0             |
| Disturbance in attention    |               |                |               |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)           | 0             | 0              | 0             |
| Dizziness                   |               |                |               |

|                               |                |                |               |
|-------------------------------|----------------|----------------|---------------|
| subjects affected / exposed   | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)             | 0              | 0              | 0             |
| Dizziness postural            |                |                |               |
| subjects affected / exposed   | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)             | 0              | 0              | 0             |
| Headache                      |                |                |               |
| subjects affected / exposed   | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)             | 0              | 0              | 0             |
| Dysgeusia                     |                |                |               |
| subjects affected / exposed   | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)             | 0              | 0              | 0             |
| Motor dysfunction             |                |                |               |
| subjects affected / exposed   | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)             | 0              | 0              | 0             |
| Neuropathy peripheral         |                |                |               |
| subjects affected / exposed   | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)             | 0              | 0              | 0             |
| Peripheral sensory neuropathy |                |                |               |
| subjects affected / exposed   | 1 / 2 (50.00%) | 0 / 2 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)             | 1              | 0              | 0             |
| Paraesthesia                  |                |                |               |
| subjects affected / exposed   | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)             | 0              | 0              | 0             |
| Presyncope                    |                |                |               |
| subjects affected / exposed   | 0 / 2 (0.00%)  | 1 / 2 (50.00%) | 0 / 4 (0.00%) |
| occurrences (all)             | 0              | 1              | 0             |
| Radiculopathy                 |                |                |               |
| subjects affected / exposed   | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)             | 0              | 0              | 0             |
| Syncope                       |                |                |               |
| subjects affected / exposed   | 0 / 2 (0.00%)  | 1 / 2 (50.00%) | 0 / 4 (0.00%) |
| occurrences (all)             | 0              | 1              | 0             |
| Somnolence                    |                |                |               |
| subjects affected / exposed   | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)             | 0              | 0              | 0             |
| Sciatica                      |                |                |               |

|  |                     |                      |                      |
|--|---------------------|----------------------|----------------------|
| subjects affected / exposed<br>occurrences (all)                           | 0 / 2 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0   | 0 / 4 (0.00%)<br>0   |
| Taste disorder<br>subjects affected / exposed<br>occurrences (all)         | 0 / 2 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0   | 0 / 4 (0.00%)<br>0   |
| Blood and lymphatic system disorders                                       |                     |                      |                      |
| Anaemia<br>subjects affected / exposed<br>occurrences (all)                | 1 / 2 (50.00%)<br>1 | 1 / 2 (50.00%)<br>1  | 0 / 4 (0.00%)<br>0   |
| Coagulopathy<br>subjects affected / exposed<br>occurrences (all)           | 0 / 2 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0   | 0 / 4 (0.00%)<br>0   |
| Eosinophilia<br>subjects affected / exposed<br>occurrences (all)           | 0 / 2 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0   | 0 / 4 (0.00%)<br>0   |
| Lymph node haemorrhage<br>subjects affected / exposed<br>occurrences (all) | 0 / 2 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0   | 0 / 4 (0.00%)<br>0   |
| Lymph node pain<br>subjects affected / exposed<br>occurrences (all)        | 0 / 2 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0   | 0 / 4 (0.00%)<br>0   |
| Lymphadenopathy<br>subjects affected / exposed<br>occurrences (all)        | 0 / 2 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0   | 0 / 4 (0.00%)<br>0   |
| Neutropenia<br>subjects affected / exposed<br>occurrences (all)            | 0 / 2 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0   | 2 / 4 (50.00%)<br>3  |
| Lymphopenia<br>subjects affected / exposed<br>occurrences (all)            | 0 / 2 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0   | 0 / 4 (0.00%)<br>0   |
| Thrombocytopenia<br>subjects affected / exposed<br>occurrences (all)       | 0 / 2 (0.00%)<br>0  | 2 / 2 (100.00%)<br>8 | 4 / 4 (100.00%)<br>9 |
| Ear and labyrinth disorders<br>Ear congestion                              |                     |                      |                      |

|  |                     |                     |                     |
|--|---------------------|---------------------|---------------------|
| subjects affected / exposed<br>occurrences (all)   | 0 / 2 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0  |
| Ear haemorrhage<br>subjects affected / exposed<br>occurrences (all)                                    | 0 / 2 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0  |
| Ear pain<br>subjects affected / exposed<br>occurrences (all)   | 0 / 2 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0  |
| Vertigo<br>subjects affected / exposed<br>occurrences (all)  | 0 / 2 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0  |
| Eye disorders<br>Conjunctival haemorrhage<br>subjects affected / exposed<br>occurrences (all)          | 0 / 2 (0.00%)<br>0  | 1 / 2 (50.00%)<br>1 | 0 / 4 (0.00%)<br>0  |
| Dry eye<br>subjects affected / exposed<br>occurrences (all)  | 0 / 2 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0  |
| Vitreous haemorrhage<br>subjects affected / exposed<br>occurrences (all)                               | 0 / 2 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0  |
| Vision blurred<br>subjects affected / exposed<br>occurrences (all)                                     | 0 / 2 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0  |
| Periorbital oedema<br>subjects affected / exposed<br>occurrences (all)                                 | 0 / 2 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0  |
| Gastrointestinal disorders<br>Abdominal pain upper<br>subjects affected / exposed<br>occurrences (all) | 1 / 2 (50.00%)<br>1 | 0 / 2 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0  |
| Abdominal pain<br>subjects affected / exposed<br>occurrences (all)                                     | 0 / 2 (0.00%)<br>0  | 0 / 2 (0.00%)<br>0  | 1 / 4 (25.00%)<br>1 |
| Abdominal distension   |                     |                     |                     |

|                             |                 |                 |                |
|-----------------------------|-----------------|-----------------|----------------|
| subjects affected / exposed | 0 / 2 (0.00%)   | 1 / 2 (50.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)           | 0               | 1               | 0              |
| Anal fissure                |                 |                 |                |
| subjects affected / exposed | 0 / 2 (0.00%)   | 0 / 2 (0.00%)   | 0 / 4 (0.00%)  |
| occurrences (all)           | 0               | 0               | 0              |
| Anal haemorrhage            |                 |                 |                |
| subjects affected / exposed | 0 / 2 (0.00%)   | 0 / 2 (0.00%)   | 0 / 4 (0.00%)  |
| occurrences (all)           | 0               | 0               | 0              |
| Aphthous ulcer              |                 |                 |                |
| subjects affected / exposed | 0 / 2 (0.00%)   | 0 / 2 (0.00%)   | 0 / 4 (0.00%)  |
| occurrences (all)           | 0               | 0               | 0              |
| Angular cheilitis           |                 |                 |                |
| subjects affected / exposed | 0 / 2 (0.00%)   | 0 / 2 (0.00%)   | 0 / 4 (0.00%)  |
| occurrences (all)           | 0               | 0               | 0              |
| Anal inflammation           |                 |                 |                |
| subjects affected / exposed | 0 / 2 (0.00%)   | 0 / 2 (0.00%)   | 0 / 4 (0.00%)  |
| occurrences (all)           | 0               | 0               | 0              |
| Ascites                     |                 |                 |                |
| subjects affected / exposed | 0 / 2 (0.00%)   | 0 / 2 (0.00%)   | 0 / 4 (0.00%)  |
| occurrences (all)           | 0               | 0               | 0              |
| Constipation                |                 |                 |                |
| subjects affected / exposed | 0 / 2 (0.00%)   | 0 / 2 (0.00%)   | 0 / 4 (0.00%)  |
| occurrences (all)           | 0               | 0               | 0              |
| Diarrhoea                   |                 |                 |                |
| subjects affected / exposed | 2 / 2 (100.00%) | 2 / 2 (100.00%) | 3 / 4 (75.00%) |
| occurrences (all)           | 3               | 2               | 3              |
| Dry mouth                   |                 |                 |                |
| subjects affected / exposed | 0 / 2 (0.00%)   | 0 / 2 (0.00%)   | 0 / 4 (0.00%)  |
| occurrences (all)           | 0               | 0               | 0              |
| Dyspepsia                   |                 |                 |                |
| subjects affected / exposed | 0 / 2 (0.00%)   | 0 / 2 (0.00%)   | 0 / 4 (0.00%)  |
| occurrences (all)           | 0               | 0               | 0              |
| Dysphagia                   |                 |                 |                |
| subjects affected / exposed | 0 / 2 (0.00%)   | 0 / 2 (0.00%)   | 0 / 4 (0.00%)  |
| occurrences (all)           | 0               | 0               | 0              |
| Flatulence                  |                 |                 |                |

|                                    |                |                |                |
|------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed        | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                  | 0              | 0              | 0              |
| Gastritis                          |                |                |                |
| subjects affected / exposed        | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                  | 0              | 0              | 0              |
| Gastritis erosive                  |                |                |                |
| subjects affected / exposed        | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                  | 0              | 0              | 0              |
| Gastrointestinal disorder          |                |                |                |
| subjects affected / exposed        | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                  | 0              | 0              | 0              |
| Gastrooesophageal reflux disease   |                |                |                |
| subjects affected / exposed        | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                  | 0              | 0              | 0              |
| Haemorrhoids                       |                |                |                |
| subjects affected / exposed        | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                  | 0              | 0              | 0              |
| Lip dry                            |                |                |                |
| subjects affected / exposed        | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                  | 0              | 0              | 0              |
| Melaena                            |                |                |                |
| subjects affected / exposed        | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 1 / 4 (25.00%) |
| occurrences (all)                  | 0              | 0              | 1              |
| Lower gastrointestinal haemorrhage |                |                |                |
| subjects affected / exposed        | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                  | 0              | 0              | 0              |
| Nausea                             |                |                |                |
| subjects affected / exposed        | 1 / 2 (50.00%) | 1 / 2 (50.00%) | 2 / 4 (50.00%) |
| occurrences (all)                  | 1              | 1              | 3              |
| Odynophagia                        |                |                |                |
| subjects affected / exposed        | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                  | 0              | 0              | 0              |
| Oral mucosal erythema              |                |                |                |
| subjects affected / exposed        | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)                  | 0              | 0              | 0              |
| Retching                           |                |                |                |



|  |                |               |                |
|--|----------------|---------------|----------------|
| subjects affected / exposed            | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 4 (0.00%)  |
| occurrences (all)                      | 0              | 0             | 0              |
| Stomatitis                             |                |               |                |
| subjects affected / exposed            | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 4 (0.00%)  |
| occurrences (all)                      | 0              | 0             | 0              |
| Subileus                               |                |               |                |
| subjects affected / exposed            | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 4 (0.00%)  |
| occurrences (all)                      | 0              | 0             | 0              |
| Toothache                              |                |               |                |
| subjects affected / exposed            | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 4 (0.00%)  |
| occurrences (all)                      | 0              | 0             | 0              |
| Vomiting                               |                |               |                |
| subjects affected / exposed            | 1 / 2 (50.00%) | 0 / 2 (0.00%) | 1 / 4 (25.00%) |
| occurrences (all)                      | 1              | 0             | 1              |
| Hepatobiliary disorders                |                |               |                |
| Cholangitis                            |                |               |                |
| subjects affected / exposed            | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 4 (0.00%)  |
| occurrences (all)                      | 0              | 0             | 0              |
| Hepatic cytolysis                      |                |               |                |
| subjects affected / exposed            | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 4 (0.00%)  |
| occurrences (all)                      | 0              | 0             | 0              |
| Hepatic pain                           |                |               |                |
| subjects affected / exposed            | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 4 (0.00%)  |
| occurrences (all)                      | 0              | 0             | 0              |
| Skin and subcutaneous tissue disorders |                |               |                |
| Dermatitis psoriasiform                |                |               |                |
| subjects affected / exposed            | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 4 (0.00%)  |
| occurrences (all)                      | 0              | 0             | 0              |
| Dermatitis acneiform                   |                |               |                |
| subjects affected / exposed            | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 4 (0.00%)  |
| occurrences (all)                      | 0              | 0             | 0              |
| Dry skin                               |                |               |                |
| subjects affected / exposed            | 0 / 2 (0.00%)  | 0 / 2 (0.00%) | 0 / 4 (0.00%)  |
| occurrences (all)                      | 0              | 0             | 0              |
| Intertrigo                             |                |               |                |

|                             |               |                |               |
|-----------------------------|---------------|----------------|---------------|
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)           | 0             | 0              | 0             |
| Macule                      |               |                |               |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)           | 0             | 0              | 0             |
| Night sweats                |               |                |               |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)           | 0             | 0              | 0             |
| Eczema                      |               |                |               |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)           | 0             | 0              | 0             |
| Erythema                    |               |                |               |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)           | 0             | 0              | 0             |
| Prurigo                     |               |                |               |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)           | 0             | 0              | 0             |
| Pruritus                    |               |                |               |
| subjects affected / exposed | 0 / 2 (0.00%) | 1 / 2 (50.00%) | 0 / 4 (0.00%) |
| occurrences (all)           | 0             | 1              | 0             |
| Psoriasis                   |               |                |               |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)           | 0             | 0              | 0             |
| Petechiae                   |               |                |               |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)           | 0             | 0              | 0             |
| Skin ulcer                  |               |                |               |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)           | 0             | 0              | 0             |
| Rash                        |               |                |               |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)           | 0             | 0              | 0             |
| Rash maculo-papular         |               |                |               |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 2 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)           | 0             | 0              | 0             |
| Purpura                     |               |                |               |

|   |                |                |               |
|---|----------------|----------------|---------------|
| subjects affected / exposed                     | 0 / 2 (0.00%)  | 1 / 2 (50.00%) | 0 / 4 (0.00%) |
| occurrences (all)                               | 0              | 1              | 0             |
| Urticaria                                       |                |                |               |
| subjects affected / exposed                     | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)                               | 0              | 0              | 0             |
| Renal and urinary disorders                     |                |                |               |
| Dysuria   |                |                |               |
| subjects affected / exposed                     | 0 / 2 (0.00%)  | 1 / 2 (50.00%) | 0 / 4 (0.00%) |
| occurrences (all)                               | 0              | 1              | 0             |
| Haematuria                                      |                |                |               |
| subjects affected / exposed                     | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)                               | 0              | 0              | 0             |
| Pollakiuria                                     |                |                |               |
| subjects affected / exposed                     | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)                               | 0              | 0              | 0             |
| Urinary tract pain                              |                |                |               |
| subjects affected / exposed                     | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)                               | 0              | 0              | 0             |
| Urinary retention                               |                |                |               |
| subjects affected / exposed                     | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)                               | 0              | 0              | 0             |
| Renal failure                                   |                |                |               |
| subjects affected / exposed                     | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)                               | 0              | 0              | 0             |
| Endocrine disorders                             |                |                |               |
| Hyperthyroidism                                 |                |                |               |
| subjects affected / exposed                     | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)                               | 0              | 0              | 0             |
| Musculoskeletal and connective tissue disorders |                |                |               |
| Arthralgia                                      |                |                |               |
| subjects affected / exposed                     | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)                               | 0              | 0              | 0             |
| Back pain                                       |                |                |               |
| subjects affected / exposed                     | 1 / 2 (50.00%) | 0 / 2 (0.00%)  | 0 / 4 (0.00%) |
| occurrences (all)                               | 1              | 0              | 0             |
| Bone pain                                       |                |                |               |

|                             |                |                |                |
|-----------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0              |
| Flank pain                  |                |                |                |
| subjects affected / exposed | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0              |
| Groin pain                  |                |                |                |
| subjects affected / exposed | 0 / 2 (0.00%)  | 1 / 2 (50.00%) | 0 / 4 (0.00%)  |
| occurrences (all)           | 0              | 1              | 0              |
| Muscular weakness           |                |                |                |
| subjects affected / exposed | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0              |
| Muscle spasms               |                |                |                |
| subjects affected / exposed | 0 / 2 (0.00%)  | 1 / 2 (50.00%) | 0 / 4 (0.00%)  |
| occurrences (all)           | 0              | 1              | 0              |
| Myalgia                     |                |                |                |
| subjects affected / exposed | 1 / 2 (50.00%) | 0 / 2 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)           | 2              | 0              | 0              |
| Neck pain                   |                |                |                |
| subjects affected / exposed | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 1 / 4 (25.00%) |
| occurrences (all)           | 0              | 0              | 2              |
| Pain in extremity           |                |                |                |
| subjects affected / exposed | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0              |
| Pubic pain                  |                |                |                |
| subjects affected / exposed | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0              |
| Infections and infestations |                |                |                |
| Bronchitis                  |                |                |                |
| subjects affected / exposed | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0              |
| Bronchitis viral            |                |                |                |
| subjects affected / exposed | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0              |
| Clostridial infection       |                |                |                |
| subjects affected / exposed | 0 / 2 (0.00%)  | 0 / 2 (0.00%)  | 0 / 4 (0.00%)  |
| occurrences (all)           | 0              | 0              | 0              |

|                                     |               |               |                |
|-------------------------------------|---------------|---------------|----------------|
| Clostridium difficile colitis       |               |               |                |
| subjects affected / exposed         | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%)  |
| occurrences (all)                   | 0             | 0             | 0              |
| Conjunctivitis                      |               |               |                |
| subjects affected / exposed         | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 1 / 4 (25.00%) |
| occurrences (all)                   | 0             | 0             | 1              |
| Erysipelas                          |               |               |                |
| subjects affected / exposed         | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%)  |
| occurrences (all)                   | 0             | 0             | 0              |
| Diverticulitis                      |               |               |                |
| subjects affected / exposed         | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 1 / 4 (25.00%) |
| occurrences (all)                   | 0             | 0             | 1              |
| Cystitis                            |               |               |                |
| subjects affected / exposed         | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%)  |
| occurrences (all)                   | 0             | 0             | 0              |
| Gastroenteritis                     |               |               |                |
| subjects affected / exposed         | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%)  |
| occurrences (all)                   | 0             | 0             | 0              |
| Folliculitis                        |               |               |                |
| subjects affected / exposed         | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%)  |
| occurrences (all)                   | 0             | 0             | 0              |
| Escherichia urinary tract infection |               |               |                |
| subjects affected / exposed         | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%)  |
| occurrences (all)                   | 0             | 0             | 0              |
| Genital herpes simplex              |               |               |                |
| subjects affected / exposed         | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%)  |
| occurrences (all)                   | 0             | 0             | 0              |
| Genital infection fungal            |               |               |                |
| subjects affected / exposed         | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%)  |
| occurrences (all)                   | 0             | 0             | 0              |
| Herpes dermatitis                   |               |               |                |
| subjects affected / exposed         | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%)  |
| occurrences (all)                   | 0             | 0             | 0              |
| Impetigo                            |               |               |                |
| subjects affected / exposed         | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%)  |
| occurrences (all)                   | 0             | 0             | 0              |

|                                       |               |               |               |
|---------------------------------------|---------------|---------------|---------------|
| Herpes zoster                         |               |               |               |
| subjects affected / exposed           | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all)                     | 0             | 0             | 0             |
| Influenza                             |               |               |               |
| subjects affected / exposed           | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all)                     | 0             | 0             | 0             |
| Infection                             |               |               |               |
| subjects affected / exposed           | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all)                     | 0             | 0             | 0             |
| Nasopharyngitis                       |               |               |               |
| subjects affected / exposed           | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all)                     | 0             | 0             | 0             |
| Oesophageal infection                 |               |               |               |
| subjects affected / exposed           | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all)                     | 0             | 0             | 0             |
| Pharyngitis                           |               |               |               |
| subjects affected / exposed           | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all)                     | 0             | 0             | 0             |
| Oral herpes                           |               |               |               |
| subjects affected / exposed           | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all)                     | 0             | 0             | 0             |
| Pneumonia                             |               |               |               |
| subjects affected / exposed           | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all)                     | 0             | 0             | 0             |
| Rash pustular                         |               |               |               |
| subjects affected / exposed           | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all)                     | 0             | 0             | 0             |
| Respiratory tract infection           |               |               |               |
| subjects affected / exposed           | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all)                     | 0             | 0             | 0             |
| Respiratory tract infection bacterial |               |               |               |
| subjects affected / exposed           | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all)                     | 0             | 0             | 0             |
| Sinusitis                             |               |               |               |
| subjects affected / exposed           | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all)                     | 0             | 0             | 0             |

|  |                      |                     |                     |
|--|----------------------|---------------------|---------------------|
| Tooth abscess<br>subjects affected / exposed<br>occurrences (all)                                  | 0 / 2 (0.00%)<br>0   | 0 / 2 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0  |
| Tooth infection<br>subjects affected / exposed<br>occurrences (all)                                | 0 / 2 (0.00%)<br>0   | 0 / 2 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0  |
| Tracheitis<br>subjects affected / exposed<br>occurrences (all)                                     | 0 / 2 (0.00%)<br>0   | 0 / 2 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0  |
| Upper respiratory tract infection<br>subjects affected / exposed<br>occurrences (all)              | 1 / 2 (50.00%)<br>1  | 0 / 2 (0.00%)<br>0  | 1 / 4 (25.00%)<br>1 |
| Urinary tract infection enterococcal<br>subjects affected / exposed<br>occurrences (all)           | 0 / 2 (0.00%)<br>0   | 0 / 2 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0  |
| Urinary tract infection<br>subjects affected / exposed<br>occurrences (all)                        | 0 / 2 (0.00%)<br>0   | 1 / 2 (50.00%)<br>1 | 0 / 4 (0.00%)<br>0  |
| Mucosal infection<br>subjects affected / exposed<br>occurrences (all)                              | 0 / 2 (0.00%)<br>0   | 0 / 2 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0  |
| Stoma site infection<br>subjects affected / exposed<br>occurrences (all)                           | 0 / 2 (0.00%)<br>0   | 0 / 2 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0  |
| Metabolism and nutrition disorders<br>Acidosis<br>subjects affected / exposed<br>occurrences (all) | 0 / 2 (0.00%)<br>0   | 0 / 2 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0  |
| Decreased appetite<br>subjects affected / exposed<br>occurrences (all)                             | 2 / 2 (100.00%)<br>3 | 1 / 2 (50.00%)<br>1 | 2 / 4 (50.00%)<br>2 |
| Cell death<br>subjects affected / exposed<br>occurrences (all)                                     | 0 / 2 (0.00%)<br>0   | 0 / 2 (0.00%)<br>0  | 0 / 4 (0.00%)<br>0  |
| Dehydration  |                      |                     |                     |

|                             |               |               |               |
|-----------------------------|---------------|---------------|---------------|
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all)           | 0             | 0             | 0             |
| Fluid retention             |               |               |               |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all)           | 0             | 0             | 0             |
| Folate deficiency           |               |               |               |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all)           | 0             | 0             | 0             |
| Gout                        |               |               |               |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all)           | 0             | 0             | 0             |
| Hypercalcaemia              |               |               |               |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all)           | 0             | 0             | 0             |
| Hyperkalaemia               |               |               |               |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all)           | 0             | 0             | 0             |
| Hyperglycaemia              |               |               |               |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all)           | 0             | 0             | 0             |
| Hyperphosphataemia          |               |               |               |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all)           | 0             | 0             | 0             |
| Hypoalbuminaemia            |               |               |               |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all)           | 0             | 0             | 0             |
| Hypocalcaemia               |               |               |               |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all)           | 0             | 0             | 0             |
| Hypokalaemia                |               |               |               |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all)           | 0             | 0             | 0             |
| Hypomagnesaemia             |               |               |               |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all)           | 0             | 0             | 0             |
| Hyponatraemia               |               |               |               |



|                             |               |               |               |
|-----------------------------|---------------|---------------|---------------|
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all)           | 0             | 0             | 0             |
| Hypophosphataemia           |               |               |               |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all)           | 0             | 0             | 0             |
| Malnutrition                |               |               |               |
| subjects affected / exposed | 0 / 2 (0.00%) | 0 / 2 (0.00%) | 0 / 4 (0.00%) |
| occurrences (all)           | 0             | 0             | 0             |

| <b>Non-serious adverse events</b>                                   | Phase Ib - Schedule B: 2 mg BI 894999 (SCLC patients) | Phase Ib - Schedule C: BI 894999 6/3 mg (NC patients) | Phase Ib - Schedule B: 2.5 mg BI 894999 (NC patients) |
|---|---|---|---|
| Total subjects affected by non-serious adverse events               |   |   |   |
| subjects affected / exposed   | 9 / 9 (100.00%)                                       | 21 / 21 (100.00%)                                     | 20 / 20 (100.00%)                                     |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |   |   |   |
| Tumour pain   |   |   |   |
| subjects affected / exposed   | 0 / 9 (0.00%)   | 2 / 21 (9.52%)  | 2 / 20 (10.00%)                                       |
| occurrences (all)   | 0   | 3   | 3   |
| Vascular disorders  |   |   |   |
| Hypotension   |   |   |   |
| subjects affected / exposed   | 0 / 9 (0.00%)   | 0 / 21 (0.00%)  | 0 / 20 (0.00%)  |
| occurrences (all)   | 0   | 0   | 0   |
| Hypertension  |   |   |   |
| subjects affected / exposed   | 0 / 9 (0.00%)   | 4 / 21 (19.05%)                                       | 0 / 20 (0.00%)  |
| occurrences (all)   | 0   | 4   | 0   |
| Haematoma   |   |   |   |
| subjects affected / exposed   | 0 / 9 (0.00%)   | 0 / 21 (0.00%)  | 0 / 20 (0.00%)  |
| occurrences (all)   | 0   | 0   | 0   |
| Orthostatic hypotension   |   |   |   |
| subjects affected / exposed   | 0 / 9 (0.00%)   | 0 / 21 (0.00%)  | 0 / 20 (0.00%)  |
| occurrences (all)   | 0   | 0   | 0   |
| Pallor  |   |   |   |
| subjects affected / exposed   | 0 / 9 (0.00%)   | 0 / 21 (0.00%)  | 0 / 20 (0.00%)  |
| occurrences (all)   | 0   | 0   | 0   |
| General disorders and administration site conditions                |   |   |   |

|                                       |                |                  |                 |
|---------------------------------------|----------------|------------------|-----------------|
| Chest discomfort                      |                |                  |                 |
| subjects affected / exposed           | 0 / 9 (0.00%)  | 0 / 21 (0.00%)   | 0 / 20 (0.00%)  |
| occurrences (all)                     | 0              | 0                | 0               |
| Asthenia                              |                |                  |                 |
| subjects affected / exposed           | 1 / 9 (11.11%) | 2 / 21 (9.52%)   | 1 / 20 (5.00%)  |
| occurrences (all)                     | 1              | 3                | 1               |
| Chest pain                            |                |                  |                 |
| subjects affected / exposed           | 0 / 9 (0.00%)  | 1 / 21 (4.76%)   | 0 / 20 (0.00%)  |
| occurrences (all)                     | 0              | 2                | 0               |
| Fatigue                               |                |                  |                 |
| subjects affected / exposed           | 3 / 9 (33.33%) | 10 / 21 (47.62%) | 8 / 20 (40.00%) |
| occurrences (all)                     | 3              | 14               | 11              |
| Facial pain                           |                |                  |                 |
| subjects affected / exposed           | 0 / 9 (0.00%)  | 0 / 21 (0.00%)   | 0 / 20 (0.00%)  |
| occurrences (all)                     | 0              | 0                | 0               |
| Chills                                |                |                  |                 |
| subjects affected / exposed           | 0 / 9 (0.00%)  | 0 / 21 (0.00%)   | 0 / 20 (0.00%)  |
| occurrences (all)                     | 0              | 0                | 0               |
| Gait disturbance                      |                |                  |                 |
| subjects affected / exposed           | 0 / 9 (0.00%)  | 0 / 21 (0.00%)   | 0 / 20 (0.00%)  |
| occurrences (all)                     | 0              | 0                | 0               |
| General physical health deterioration |                |                  |                 |
| subjects affected / exposed           | 0 / 9 (0.00%)  | 0 / 21 (0.00%)   | 0 / 20 (0.00%)  |
| occurrences (all)                     | 0              | 0                | 0               |
| Generalised oedema                    |                |                  |                 |
| subjects affected / exposed           | 0 / 9 (0.00%)  | 0 / 21 (0.00%)   | 0 / 20 (0.00%)  |
| occurrences (all)                     | 0              | 0                | 0               |
| Malaise                               |                |                  |                 |
| subjects affected / exposed           | 0 / 9 (0.00%)  | 0 / 21 (0.00%)   | 0 / 20 (0.00%)  |
| occurrences (all)                     | 0              | 0                | 0               |
| Hypothermia                           |                |                  |                 |
| subjects affected / exposed           | 0 / 9 (0.00%)  | 0 / 21 (0.00%)   | 0 / 20 (0.00%)  |
| occurrences (all)                     | 0              | 0                | 0               |
| Oedema peripheral                     |                |                  |                 |
| subjects affected / exposed           | 1 / 9 (11.11%) | 1 / 21 (4.76%)   | 0 / 20 (0.00%)  |
| occurrences (all)                     | 1              | 3                | 0               |

|  |                     |                      |                      |
|--|---------------------|----------------------|----------------------|
| Non-cardiac chest pain<br>subjects affected / exposed<br>occurrences (all)   | 0 / 9 (0.00%)<br>0  | 0 / 21 (0.00%)<br>0  | 1 / 20 (5.00%)<br>1  |
| Pain<br>subjects affected / exposed<br>occurrences (all)   | 0 / 9 (0.00%)<br>0  | 1 / 21 (4.76%)<br>1  | 1 / 20 (5.00%)<br>1  |
| Pyrexia<br>subjects affected / exposed<br>occurrences (all)  | 0 / 9 (0.00%)<br>0  | 5 / 21 (23.81%)<br>6 | 4 / 20 (20.00%)<br>7 |
| Peripheral swelling<br>subjects affected / exposed<br>occurrences (all)  | 0 / 9 (0.00%)<br>0  | 0 / 21 (0.00%)<br>0  | 0 / 20 (0.00%)<br>0  |
| Immune system disorders<br>Hypersensitivity<br>subjects affected / exposed<br>occurrences (all)                      | 1 / 9 (11.11%)<br>1 | 0 / 21 (0.00%)<br>0  | 0 / 20 (0.00%)<br>0  |
| Iodine allergy<br>subjects affected / exposed<br>occurrences (all)   | 0 / 9 (0.00%)<br>0  | 0 / 21 (0.00%)<br>0  | 0 / 20 (0.00%)<br>0  |
| Reproductive system and breast disorders<br>Erectile dysfunction<br>subjects affected / exposed<br>occurrences (all) | 0 / 9 (0.00%)<br>0  | 0 / 21 (0.00%)<br>0  | 0 / 20 (0.00%)<br>0  |
| Heavy menstrual bleeding<br>subjects affected / exposed<br>occurrences (all)   | 0 / 9 (0.00%)<br>0  | 0 / 21 (0.00%)<br>0  | 0 / 20 (0.00%)<br>0  |
| Oedema genital<br>subjects affected / exposed<br>occurrences (all)   | 0 / 9 (0.00%)<br>0  | 1 / 21 (4.76%)<br>1  | 0 / 20 (0.00%)<br>0  |
| Perineal pain<br>subjects affected / exposed<br>occurrences (all)  | 0 / 9 (0.00%)<br>0  | 0 / 21 (0.00%)<br>0  | 0 / 20 (0.00%)<br>0  |
| Scrotal oedema<br>subjects affected / exposed<br>occurrences (all)   | 0 / 9 (0.00%)<br>0  | 0 / 21 (0.00%)<br>0  | 0 / 20 (0.00%)<br>0  |
| Testicular pain  |                     |                      |                      |

|   |                |                 |                 |
|---|----------------|-----------------|-----------------|
| subjects affected / exposed                     | 0 / 9 (0.00%)  | 0 / 21 (0.00%)  | 0 / 20 (0.00%)  |
| occurrences (all)                               | 0              | 0               | 0               |
| Vulvovaginal discomfort                         |                |                 |                 |
| subjects affected / exposed                     | 0 / 9 (0.00%)  | 0 / 21 (0.00%)  | 0 / 20 (0.00%)  |
| occurrences (all)                               | 0              | 0               | 0               |
| Vaginal haemorrhage                             |                |                 |                 |
| subjects affected / exposed                     | 0 / 9 (0.00%)  | 0 / 21 (0.00%)  | 0 / 20 (0.00%)  |
| occurrences (all)                               | 0              | 0               | 0               |
| Respiratory, thoracic and mediastinal disorders |                |                 |                 |
| Atelectasis                                     |                |                 |                 |
| subjects affected / exposed                     | 0 / 9 (0.00%)  | 0 / 21 (0.00%)  | 0 / 20 (0.00%)  |
| occurrences (all)                               | 0              | 0               | 0               |
| Dysphonia                                       |                |                 |                 |
| subjects affected / exposed                     | 1 / 9 (11.11%) | 0 / 21 (0.00%)  | 0 / 20 (0.00%)  |
| occurrences (all)                               | 1              | 0               | 0               |
| Cough   |                |                 |                 |
| subjects affected / exposed                     | 3 / 9 (33.33%) | 5 / 21 (23.81%) | 2 / 20 (10.00%) |
| occurrences (all)                               | 3              | 7               | 2               |
| Dyspnoea  |                |                 |                 |
| subjects affected / exposed                     | 4 / 9 (44.44%) | 1 / 21 (4.76%)  | 3 / 20 (15.00%) |
| occurrences (all)                               | 5              | 1               | 4               |
| Dyspnoea exertional                             |                |                 |                 |
| subjects affected / exposed                     | 0 / 9 (0.00%)  | 0 / 21 (0.00%)  | 0 / 20 (0.00%)  |
| occurrences (all)                               | 0              | 0               | 0               |
| Epistaxis                                       |                |                 |                 |
| subjects affected / exposed                     | 0 / 9 (0.00%)  | 4 / 21 (19.05%) | 2 / 20 (10.00%) |
| occurrences (all)                               | 0              | 5               | 2               |
| Laryngeal inflammation                          |                |                 |                 |
| subjects affected / exposed                     | 0 / 9 (0.00%)  | 0 / 21 (0.00%)  | 0 / 20 (0.00%)  |
| occurrences (all)                               | 0              | 0               | 0               |
| Haemoptysis                                     |                |                 |                 |
| subjects affected / exposed                     | 1 / 9 (11.11%) | 1 / 21 (4.76%)  | 1 / 20 (5.00%)  |
| occurrences (all)                               | 1              | 1               | 1               |
| Nasal discomfort                                |                |                 |                 |

|                              |               |                |                 |
|------------------------------|---------------|----------------|-----------------|
| subjects affected / exposed  | 0 / 9 (0.00%) | 0 / 21 (0.00%) | 0 / 20 (0.00%)  |
| occurrences (all)            | 0             | 0              | 0               |
| Oropharyngeal pain           |               |                |                 |
| subjects affected / exposed  | 0 / 9 (0.00%) | 1 / 21 (4.76%) | 1 / 20 (5.00%)  |
| occurrences (all)            | 0             | 1              | 1               |
| Pharyngeal inflammation      |               |                |                 |
| subjects affected / exposed  | 0 / 9 (0.00%) | 0 / 21 (0.00%) | 0 / 20 (0.00%)  |
| occurrences (all)            | 0             | 0              | 0               |
| Pleural effusion             |               |                |                 |
| subjects affected / exposed  | 0 / 9 (0.00%) | 0 / 21 (0.00%) | 0 / 20 (0.00%)  |
| occurrences (all)            | 0             | 0              | 0               |
| Pleuritic pain               |               |                |                 |
| subjects affected / exposed  | 0 / 9 (0.00%) | 0 / 21 (0.00%) | 0 / 20 (0.00%)  |
| occurrences (all)            | 0             | 0              | 0               |
| Productive cough             |               |                |                 |
| subjects affected / exposed  | 0 / 9 (0.00%) | 1 / 21 (4.76%) | 0 / 20 (0.00%)  |
| occurrences (all)            | 0             | 1              | 0               |
| Rhinorrhoea                  |               |                |                 |
| subjects affected / exposed  | 0 / 9 (0.00%) | 0 / 21 (0.00%) | 0 / 20 (0.00%)  |
| occurrences (all)            | 0             | 0              | 0               |
| Respiratory tract congestion |               |                |                 |
| subjects affected / exposed  | 0 / 9 (0.00%) | 0 / 21 (0.00%) | 0 / 20 (0.00%)  |
| occurrences (all)            | 0             | 0              | 0               |
| Wheezing                     |               |                |                 |
| subjects affected / exposed  | 0 / 9 (0.00%) | 0 / 21 (0.00%) | 1 / 20 (5.00%)  |
| occurrences (all)            | 0             | 0              | 1               |
| Psychiatric disorders        |               |                |                 |
| Affective disorder           |               |                |                 |
| subjects affected / exposed  | 0 / 9 (0.00%) | 0 / 21 (0.00%) | 0 / 20 (0.00%)  |
| occurrences (all)            | 0             | 0              | 0               |
| Agitation                    |               |                |                 |
| subjects affected / exposed  | 0 / 9 (0.00%) | 0 / 21 (0.00%) | 0 / 20 (0.00%)  |
| occurrences (all)            | 0             | 0              | 0               |
| Anxiety                      |               |                |                 |
| subjects affected / exposed  | 0 / 9 (0.00%) | 0 / 21 (0.00%) | 4 / 20 (20.00%) |
| occurrences (all)            | 0             | 0              | 4               |

|   |                |                 |                 |
|---|----------------|-----------------|-----------------|
| Confusional state                               |                |                 |                 |
| subjects affected / exposed                     | 0 / 9 (0.00%)  | 0 / 21 (0.00%)  | 0 / 20 (0.00%)  |
| occurrences (all)                               | 0              | 0               | 0               |
| Depression                                      |                |                 |                 |
| subjects affected / exposed                     | 0 / 9 (0.00%)  | 0 / 21 (0.00%)  | 0 / 20 (0.00%)  |
| occurrences (all)                               | 0              | 0               | 0               |
| Insomnia  |                |                 |                 |
| subjects affected / exposed                     | 0 / 9 (0.00%)  | 0 / 21 (0.00%)  | 1 / 20 (5.00%)  |
| occurrences (all)                               | 0              | 0               | 1               |
| Hallucination                                   |                |                 |                 |
| subjects affected / exposed                     | 0 / 9 (0.00%)  | 0 / 21 (0.00%)  | 0 / 20 (0.00%)  |
| occurrences (all)                               | 0              | 0               | 0               |
| Personality change                              |                |                 |                 |
| subjects affected / exposed                     | 0 / 9 (0.00%)  | 0 / 21 (0.00%)  | 0 / 20 (0.00%)  |
| occurrences (all)                               | 0              | 0               | 0               |
| Sleep disorder                                  |                |                 |                 |
| subjects affected / exposed                     | 0 / 9 (0.00%)  | 0 / 21 (0.00%)  | 1 / 20 (5.00%)  |
| occurrences (all)                               | 0              | 0               | 1               |
| Investigations                                  |                |                 |                 |
| Activated partial thromboplastin time prolonged |                |                 |                 |
| subjects affected / exposed                     | 0 / 9 (0.00%)  | 0 / 21 (0.00%)  | 1 / 20 (5.00%)  |
| occurrences (all)                               | 0              | 0               | 1               |
| Activated partial thromboplastin time shortened |                |                 |                 |
| subjects affected / exposed                     | 0 / 9 (0.00%)  | 0 / 21 (0.00%)  | 0 / 20 (0.00%)  |
| occurrences (all)                               | 0              | 0               | 0               |
| Alanine aminotransferase increased              |                |                 |                 |
| subjects affected / exposed                     | 2 / 9 (22.22%) | 4 / 21 (19.05%) | 6 / 20 (30.00%) |
| occurrences (all)                               | 2              | 7               | 8               |
| Aspartate aminotransferase increased            |                |                 |                 |
| subjects affected / exposed                     | 1 / 9 (11.11%) | 1 / 21 (4.76%)  | 5 / 20 (25.00%) |
| occurrences (all)                               | 1              | 3               | 6               |
| Blood alkaline phosphatase increased            |                |                 |                 |
| subjects affected / exposed                     | 0 / 9 (0.00%)  | 1 / 21 (4.76%)  | 2 / 20 (10.00%) |
| occurrences (all)                               | 0              | 2               | 2               |
| Blood antidiuretic hormone                      |                |                 |                 |

|  |                |                |                 |
|--|----------------|----------------|-----------------|
| decreased                              |                |                |                 |
| subjects affected / exposed            | 1 / 9 (11.11%) | 0 / 21 (0.00%) | 0 / 20 (0.00%)  |
| occurrences (all)                      | 1              | 0              | 0               |
| Blood bilirubin increased              |                |                |                 |
| subjects affected / exposed            | 0 / 9 (0.00%)  | 0 / 21 (0.00%) | 2 / 20 (10.00%) |
| occurrences (all)                      | 0              | 0              | 5               |
| Blood creatine phosphokinase increased |                |                |                 |
| subjects affected / exposed            | 1 / 9 (11.11%) | 0 / 21 (0.00%) | 5 / 20 (25.00%) |
| occurrences (all)                      | 1              | 0              | 5               |
| Blood creatinine increased             |                |                |                 |
| subjects affected / exposed            | 0 / 9 (0.00%)  | 0 / 21 (0.00%) | 2 / 20 (10.00%) |
| occurrences (all)                      | 0              | 0              | 2               |
| Blood magnesium decreased              |                |                |                 |
| subjects affected / exposed            | 1 / 9 (11.11%) | 0 / 21 (0.00%) | 0 / 20 (0.00%)  |
| occurrences (all)                      | 1              | 0              | 0               |
| Blood glucose increased                |                |                |                 |
| subjects affected / exposed            | 1 / 9 (11.11%) | 0 / 21 (0.00%) | 1 / 20 (5.00%)  |
| occurrences (all)                      | 1              | 0              | 1               |
| C-reactive protein increased           |                |                |                 |
| subjects affected / exposed            | 0 / 9 (0.00%)  | 0 / 21 (0.00%) | 0 / 20 (0.00%)  |
| occurrences (all)                      | 0              | 0              | 0               |
| Cardiac murmur                         |                |                |                 |
| subjects affected / exposed            | 0 / 9 (0.00%)  | 0 / 21 (0.00%) | 0 / 20 (0.00%)  |
| occurrences (all)                      | 0              | 0              | 0               |
| Cortisol increased                     |                |                |                 |
| subjects affected / exposed            | 0 / 9 (0.00%)  | 0 / 21 (0.00%) | 0 / 20 (0.00%)  |
| occurrences (all)                      | 0              | 0              | 0               |
| Echocardiogram abnormal                |                |                |                 |
| subjects affected / exposed            | 0 / 9 (0.00%)  | 0 / 21 (0.00%) | 0 / 20 (0.00%)  |
| occurrences (all)                      | 0              | 0              | 0               |
| Electrocardiogram PR prolongation      |                |                |                 |
| subjects affected / exposed            | 1 / 9 (11.11%) | 0 / 21 (0.00%) | 0 / 20 (0.00%)  |
| occurrences (all)                      | 2              | 0              | 0               |
| Ejection fraction decreased            |                |                |                 |

|  |                |                 |                 |
|--|----------------|-----------------|-----------------|
| subjects affected / exposed              | 0 / 9 (0.00%)  | 0 / 21 (0.00%)  | 1 / 20 (5.00%)  |
| occurrences (all)                        | 0              | 0               | 1               |
| Electrocardiogram ST segment elevation   |                |                 |                 |
| subjects affected / exposed              | 0 / 9 (0.00%)  | 0 / 21 (0.00%)  | 0 / 20 (0.00%)  |
| occurrences (all)                        | 0              | 0               | 0               |
| Gamma-glutamyltransferase increased      |                |                 |                 |
| subjects affected / exposed              | 0 / 9 (0.00%)  | 0 / 21 (0.00%)  | 0 / 20 (0.00%)  |
| occurrences (all)                        | 0              | 0               | 0               |
| Electrocardiogram T wave inversion       |                |                 |                 |
| subjects affected / exposed              | 1 / 9 (11.11%) | 0 / 21 (0.00%)  | 0 / 20 (0.00%)  |
| occurrences (all)                        | 1              | 0               | 0               |
| International normalised ratio increased |                |                 |                 |
| subjects affected / exposed              | 0 / 9 (0.00%)  | 1 / 21 (4.76%)  | 5 / 20 (25.00%) |
| occurrences (all)                        | 0              | 1               | 8               |
| Lymphocyte count decreased               |                |                 |                 |
| subjects affected / exposed              | 0 / 9 (0.00%)  | 1 / 21 (4.76%)  | 0 / 20 (0.00%)  |
| occurrences (all)                        | 0              | 1               | 0               |
| Neutrophil count decreased               |                |                 |                 |
| subjects affected / exposed              | 0 / 9 (0.00%)  | 0 / 21 (0.00%)  | 1 / 20 (5.00%)  |
| occurrences (all)                        | 0              | 0               | 1               |
| Platelet count decreased                 |                |                 |                 |
| subjects affected / exposed              | 1 / 9 (11.11%) | 8 / 21 (38.10%) | 8 / 20 (40.00%) |
| occurrences (all)                        | 3              | 13              | 14              |
| Prothrombin level decreased              |                |                 |                 |
| subjects affected / exposed              | 0 / 9 (0.00%)  | 0 / 21 (0.00%)  | 0 / 20 (0.00%)  |
| occurrences (all)                        | 0              | 0               | 0               |
| Troponin I increased                     |                |                 |                 |
| subjects affected / exposed              | 0 / 9 (0.00%)  | 0 / 21 (0.00%)  | 2 / 20 (10.00%) |
| occurrences (all)                        | 0              | 0               | 2               |
| Troponin T increased                     |                |                 |                 |
| subjects affected / exposed              | 0 / 9 (0.00%)  | 1 / 21 (4.76%)  | 5 / 20 (25.00%) |
| occurrences (all)                        | 0              | 2               | 6               |
| Troponin increased                       |                |                 |                 |



|  |                |                 |                 |
|--|----------------|-----------------|-----------------|
| subjects affected / exposed                    | 0 / 9 (0.00%)  | 0 / 21 (0.00%)  | 0 / 20 (0.00%)  |
| occurrences (all)                              | 0              | 0               | 0               |
| Urine output decreased                         |                |                 |                 |
| subjects affected / exposed                    | 0 / 9 (0.00%)  | 0 / 21 (0.00%)  | 0 / 20 (0.00%)  |
| occurrences (all)                              | 0              | 0               | 0               |
| Weight decreased                               |                |                 |                 |
| subjects affected / exposed                    | 1 / 9 (11.11%) | 3 / 21 (14.29%) | 0 / 20 (0.00%)  |
| occurrences (all)                              | 1              | 3               | 0               |
| White blood cell count decreased               |                |                 |                 |
| subjects affected / exposed                    | 0 / 9 (0.00%)  | 2 / 21 (9.52%)  | 4 / 20 (20.00%) |
| occurrences (all)                              | 0              | 6               | 6               |
| Injury, poisoning and procedural complications |                |                 |                 |
| Contusion                                      |                |                 |                 |
| subjects affected / exposed                    | 0 / 9 (0.00%)  | 0 / 21 (0.00%)  | 1 / 20 (5.00%)  |
| occurrences (all)                              | 0              | 0               | 1               |
| Face injury                                    |                |                 |                 |
| subjects affected / exposed                    | 0 / 9 (0.00%)  | 0 / 21 (0.00%)  | 0 / 20 (0.00%)  |
| occurrences (all)                              | 0              | 0               | 0               |
| Infusion related reaction                      |                |                 |                 |
| subjects affected / exposed                    | 0 / 9 (0.00%)  | 0 / 21 (0.00%)  | 0 / 20 (0.00%)  |
| occurrences (all)                              | 0              | 0               | 0               |
| Limb injury                                    |                |                 |                 |
| subjects affected / exposed                    | 0 / 9 (0.00%)  | 1 / 21 (4.76%)  | 0 / 20 (0.00%)  |
| occurrences (all)                              | 0              | 1               | 0               |
| Muscle rupture                                 |                |                 |                 |
| subjects affected / exposed                    | 0 / 9 (0.00%)  | 0 / 21 (0.00%)  | 0 / 20 (0.00%)  |
| occurrences (all)                              | 0              | 0               | 0               |
| Overdose                                       |                |                 |                 |
| subjects affected / exposed                    | 0 / 9 (0.00%)  | 0 / 21 (0.00%)  | 0 / 20 (0.00%)  |
| occurrences (all)                              | 0              | 0               | 0               |
| Post procedural haematoma                      |                |                 |                 |
| subjects affected / exposed                    | 0 / 9 (0.00%)  | 0 / 21 (0.00%)  | 0 / 20 (0.00%)  |
| occurrences (all)                              | 0              | 0               | 0               |
| Skin abrasion                                  |                |                 |                 |

|                                  |                |                |                 |
|----------------------------------|----------------|----------------|-----------------|
| subjects affected / exposed      | 0 / 9 (0.00%)  | 0 / 21 (0.00%) | 0 / 20 (0.00%)  |
| occurrences (all)                | 0              | 0              | 0               |
| Procedural pain                  |                |                |                 |
| subjects affected / exposed      | 0 / 9 (0.00%)  | 0 / 21 (0.00%) | 0 / 20 (0.00%)  |
| occurrences (all)                | 0              | 0              | 0               |
| Subcutaneous haematoma           |                |                |                 |
| subjects affected / exposed      | 0 / 9 (0.00%)  | 0 / 21 (0.00%) | 0 / 20 (0.00%)  |
| occurrences (all)                | 0              | 0              | 0               |
| Skin laceration                  |                |                |                 |
| subjects affected / exposed      | 0 / 9 (0.00%)  | 0 / 21 (0.00%) | 0 / 20 (0.00%)  |
| occurrences (all)                | 0              | 0              | 0               |
| Tongue injury                    |                |                |                 |
| subjects affected / exposed      | 0 / 9 (0.00%)  | 0 / 21 (0.00%) | 0 / 20 (0.00%)  |
| occurrences (all)                | 0              | 0              | 0               |
| Tooth fracture                   |                |                |                 |
| subjects affected / exposed      | 0 / 9 (0.00%)  | 0 / 21 (0.00%) | 0 / 20 (0.00%)  |
| occurrences (all)                | 0              | 0              | 0               |
| Urinary tract stoma complication |                |                |                 |
| subjects affected / exposed      | 0 / 9 (0.00%)  | 0 / 21 (0.00%) | 0 / 20 (0.00%)  |
| occurrences (all)                | 0              | 0              | 0               |
| Cardiac disorders                |                |                |                 |
| Atrial fibrillation              |                |                |                 |
| subjects affected / exposed      | 0 / 9 (0.00%)  | 0 / 21 (0.00%) | 1 / 20 (5.00%)  |
| occurrences (all)                | 0              | 0              | 1               |
| Angina pectoris                  |                |                |                 |
| subjects affected / exposed      | 0 / 9 (0.00%)  | 0 / 21 (0.00%) | 0 / 20 (0.00%)  |
| occurrences (all)                | 0              | 0              | 0               |
| Palpitations                     |                |                |                 |
| subjects affected / exposed      | 0 / 9 (0.00%)  | 0 / 21 (0.00%) | 1 / 20 (5.00%)  |
| occurrences (all)                | 0              | 0              | 1               |
| Tachycardia                      |                |                |                 |
| subjects affected / exposed      | 1 / 9 (11.11%) | 1 / 21 (4.76%) | 1 / 20 (5.00%)  |
| occurrences (all)                | 1              | 1              | 1               |
| Sinus tachycardia                |                |                |                 |
| subjects affected / exposed      | 1 / 9 (11.11%) | 2 / 21 (9.52%) | 2 / 20 (10.00%) |
| occurrences (all)                | 1              | 2              | 2               |

|  |                     |                      |                      |
|--|---------------------|----------------------|----------------------|
| Ventricular arrhythmia<br>subjects affected / exposed<br>occurrences (all)   | 0 / 9 (0.00%)<br>0  | 1 / 21 (4.76%)<br>1  | 0 / 20 (0.00%)<br>0  |
| Nervous system disorders   |                     |                      |                      |
| Ageusia<br>subjects affected / exposed<br>occurrences (all)                  | 1 / 9 (11.11%)<br>1 | 0 / 21 (0.00%)<br>0  | 0 / 20 (0.00%)<br>0  |
| Agnosia<br>subjects affected / exposed<br>occurrences (all)                  | 0 / 9 (0.00%)<br>0  | 0 / 21 (0.00%)<br>0  | 0 / 20 (0.00%)<br>0  |
| Amnesia<br>subjects affected / exposed<br>occurrences (all)                  | 0 / 9 (0.00%)<br>0  | 0 / 21 (0.00%)<br>0  | 0 / 20 (0.00%)<br>0  |
| Cauda equina syndrome<br>subjects affected / exposed<br>occurrences (all)    | 0 / 9 (0.00%)<br>0  | 0 / 21 (0.00%)<br>0  | 0 / 20 (0.00%)<br>0  |
| Disturbance in attention<br>subjects affected / exposed<br>occurrences (all) | 0 / 9 (0.00%)<br>0  | 0 / 21 (0.00%)<br>0  | 0 / 20 (0.00%)<br>0  |
| Dizziness<br>subjects affected / exposed<br>occurrences (all)                | 0 / 9 (0.00%)<br>0  | 0 / 21 (0.00%)<br>0  | 3 / 20 (15.00%)<br>3 |
| Dizziness postural<br>subjects affected / exposed<br>occurrences (all)       | 0 / 9 (0.00%)<br>0  | 0 / 21 (0.00%)<br>0  | 0 / 20 (0.00%)<br>0  |
| Headache<br>subjects affected / exposed<br>occurrences (all)                 | 0 / 9 (0.00%)<br>0  | 2 / 21 (9.52%)<br>4  | 3 / 20 (15.00%)<br>4 |
| Dysgeusia<br>subjects affected / exposed<br>occurrences (all)                | 3 / 9 (33.33%)<br>3 | 3 / 21 (14.29%)<br>4 | 4 / 20 (20.00%)<br>5 |
| Motor dysfunction<br>subjects affected / exposed<br>occurrences (all)        | 0 / 9 (0.00%)<br>0  | 0 / 21 (0.00%)<br>0  | 0 / 20 (0.00%)<br>0  |
| Neuropathy peripheral  |                     |                      |                      |

|                                      |               |                 |                  |
|--------------------------------------|---------------|-----------------|------------------|
| subjects affected / exposed          | 0 / 9 (0.00%) | 0 / 21 (0.00%)  | 0 / 20 (0.00%)   |
| occurrences (all)                    | 0             | 0               | 0                |
| Peripheral sensory neuropathy        |               |                 |                  |
| subjects affected / exposed          | 0 / 9 (0.00%) | 0 / 21 (0.00%)  | 0 / 20 (0.00%)   |
| occurrences (all)                    | 0             | 0               | 0                |
| Paraesthesia                         |               |                 |                  |
| subjects affected / exposed          | 0 / 9 (0.00%) | 0 / 21 (0.00%)  | 1 / 20 (5.00%)   |
| occurrences (all)                    | 0             | 0               | 1                |
| Presyncope                           |               |                 |                  |
| subjects affected / exposed          | 0 / 9 (0.00%) | 0 / 21 (0.00%)  | 1 / 20 (5.00%)   |
| occurrences (all)                    | 0             | 0               | 1                |
| Radiculopathy                        |               |                 |                  |
| subjects affected / exposed          | 0 / 9 (0.00%) | 0 / 21 (0.00%)  | 0 / 20 (0.00%)   |
| occurrences (all)                    | 0             | 0               | 0                |
| Syncope                              |               |                 |                  |
| subjects affected / exposed          | 0 / 9 (0.00%) | 0 / 21 (0.00%)  | 0 / 20 (0.00%)   |
| occurrences (all)                    | 0             | 0               | 0                |
| Somnolence                           |               |                 |                  |
| subjects affected / exposed          | 0 / 9 (0.00%) | 0 / 21 (0.00%)  | 0 / 20 (0.00%)   |
| occurrences (all)                    | 0             | 0               | 0                |
| Sciatica                             |               |                 |                  |
| subjects affected / exposed          | 0 / 9 (0.00%) | 0 / 21 (0.00%)  | 0 / 20 (0.00%)   |
| occurrences (all)                    | 0             | 0               | 0                |
| Taste disorder                       |               |                 |                  |
| subjects affected / exposed          | 0 / 9 (0.00%) | 0 / 21 (0.00%)  | 1 / 20 (5.00%)   |
| occurrences (all)                    | 0             | 0               | 1                |
| Blood and lymphatic system disorders |               |                 |                  |
| Anaemia                              |               |                 |                  |
| subjects affected / exposed          | 0 / 9 (0.00%) | 6 / 21 (28.57%) | 11 / 20 (55.00%) |
| occurrences (all)                    | 0             | 10              | 18               |
| Coagulopathy                         |               |                 |                  |
| subjects affected / exposed          | 0 / 9 (0.00%) | 2 / 21 (9.52%)  | 0 / 20 (0.00%)   |
| occurrences (all)                    | 0             | 2               | 0                |
| Eosinophilia                         |               |                 |                  |
| subjects affected / exposed          | 0 / 9 (0.00%) | 0 / 21 (0.00%)  | 0 / 20 (0.00%)   |
| occurrences (all)                    | 0             | 0               | 0                |

|  |                     |                      |                       |
|--|---------------------|----------------------|-----------------------|
| Lymph node haemorrhage<br>subjects affected / exposed<br>occurrences (all)   | 0 / 9 (0.00%)<br>0  | 0 / 21 (0.00%)<br>0  | 0 / 20 (0.00%)<br>0   |
| Lymph node pain<br>subjects affected / exposed<br>occurrences (all)          | 0 / 9 (0.00%)<br>0  | 0 / 21 (0.00%)<br>0  | 0 / 20 (0.00%)<br>0   |
| Lymphadenopathy<br>subjects affected / exposed<br>occurrences (all)          | 0 / 9 (0.00%)<br>0  | 0 / 21 (0.00%)<br>0  | 0 / 20 (0.00%)<br>0   |
| Neutropenia<br>subjects affected / exposed<br>occurrences (all)              | 1 / 9 (11.11%)<br>1 | 0 / 21 (0.00%)<br>0  | 2 / 20 (10.00%)<br>3  |
| Lymphopenia<br>subjects affected / exposed<br>occurrences (all)              | 0 / 9 (0.00%)<br>0  | 0 / 21 (0.00%)<br>0  | 0 / 20 (0.00%)<br>0   |
| Thrombocytopenia<br>subjects affected / exposed<br>occurrences (all)         | 2 / 9 (22.22%)<br>2 | 5 / 21 (23.81%)<br>5 | 5 / 20 (25.00%)<br>20 |
| Ear and labyrinth disorders  |                     |                      |                       |
| Ear congestion<br>subjects affected / exposed<br>occurrences (all)           | 0 / 9 (0.00%)<br>0  | 0 / 21 (0.00%)<br>0  | 0 / 20 (0.00%)<br>0   |
| Ear haemorrhage<br>subjects affected / exposed<br>occurrences (all)          | 0 / 9 (0.00%)<br>0  | 0 / 21 (0.00%)<br>0  | 0 / 20 (0.00%)<br>0   |
| Ear pain<br>subjects affected / exposed<br>occurrences (all)                 | 0 / 9 (0.00%)<br>0  | 0 / 21 (0.00%)<br>0  | 0 / 20 (0.00%)<br>0   |
| Vertigo<br>subjects affected / exposed<br>occurrences (all)                  | 0 / 9 (0.00%)<br>0  | 0 / 21 (0.00%)<br>0  | 0 / 20 (0.00%)<br>0   |
| Eye disorders  |                     |                      |                       |
| Conjunctival haemorrhage<br>subjects affected / exposed<br>occurrences (all) | 0 / 9 (0.00%)<br>0  | 0 / 21 (0.00%)<br>0  | 0 / 20 (0.00%)<br>0   |
| Dry eye  |                     |                      |                       |

|                             |                |                 |                |
|-----------------------------|----------------|-----------------|----------------|
| subjects affected / exposed | 0 / 9 (0.00%)  | 1 / 21 (4.76%)  | 0 / 20 (0.00%) |
| occurrences (all)           | 0              | 1               | 0              |
| Vitreous haemorrhage        |                |                 |                |
| subjects affected / exposed | 0 / 9 (0.00%)  | 0 / 21 (0.00%)  | 0 / 20 (0.00%) |
| occurrences (all)           | 0              | 0               | 0              |
| Vision blurred              |                |                 |                |
| subjects affected / exposed | 0 / 9 (0.00%)  | 0 / 21 (0.00%)  | 0 / 20 (0.00%) |
| occurrences (all)           | 0              | 0               | 0              |
| Periorbital oedema          |                |                 |                |
| subjects affected / exposed | 0 / 9 (0.00%)  | 0 / 21 (0.00%)  | 0 / 20 (0.00%) |
| occurrences (all)           | 0              | 0               | 0              |
| Gastrointestinal disorders  |                |                 |                |
| Abdominal pain upper        |                |                 |                |
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 21 (0.00%)  | 0 / 20 (0.00%) |
| occurrences (all)           | 1              | 0               | 0              |
| Abdominal pain              |                |                 |                |
| subjects affected / exposed | 1 / 9 (11.11%) | 4 / 21 (19.05%) | 1 / 20 (5.00%) |
| occurrences (all)           | 1              | 5               | 1              |
| Abdominal distension        |                |                 |                |
| subjects affected / exposed | 0 / 9 (0.00%)  | 0 / 21 (0.00%)  | 1 / 20 (5.00%) |
| occurrences (all)           | 0              | 0               | 1              |
| Anal fissure                |                |                 |                |
| subjects affected / exposed | 0 / 9 (0.00%)  | 0 / 21 (0.00%)  | 0 / 20 (0.00%) |
| occurrences (all)           | 0              | 0               | 0              |
| Anal haemorrhage            |                |                 |                |
| subjects affected / exposed | 0 / 9 (0.00%)  | 0 / 21 (0.00%)  | 0 / 20 (0.00%) |
| occurrences (all)           | 0              | 0               | 0              |
| Aphthous ulcer              |                |                 |                |
| subjects affected / exposed | 0 / 9 (0.00%)  | 0 / 21 (0.00%)  | 0 / 20 (0.00%) |
| occurrences (all)           | 0              | 0               | 0              |
| Angular cheilitis           |                |                 |                |
| subjects affected / exposed | 0 / 9 (0.00%)  | 0 / 21 (0.00%)  | 0 / 20 (0.00%) |
| occurrences (all)           | 0              | 0               | 0              |
| Anal inflammation           |                |                 |                |
| subjects affected / exposed | 0 / 9 (0.00%)  | 0 / 21 (0.00%)  | 0 / 20 (0.00%) |
| occurrences (all)           | 0              | 0               | 0              |

|                                  |                |                 |                 |
|----------------------------------|----------------|-----------------|-----------------|
| Ascites                          |                |                 |                 |
| subjects affected / exposed      | 0 / 9 (0.00%)  | 1 / 21 (4.76%)  | 0 / 20 (0.00%)  |
| occurrences (all)                | 0              | 1               | 0               |
| Constipation                     |                |                 |                 |
| subjects affected / exposed      | 0 / 9 (0.00%)  | 4 / 21 (19.05%) | 5 / 20 (25.00%) |
| occurrences (all)                | 0              | 4               | 5               |
| Diarrhoea                        |                |                 |                 |
| subjects affected / exposed      | 3 / 9 (33.33%) | 9 / 21 (42.86%) | 4 / 20 (20.00%) |
| occurrences (all)                | 4              | 17              | 7               |
| Dry mouth                        |                |                 |                 |
| subjects affected / exposed      | 0 / 9 (0.00%)  | 0 / 21 (0.00%)  | 1 / 20 (5.00%)  |
| occurrences (all)                | 0              | 0               | 1               |
| Dyspepsia                        |                |                 |                 |
| subjects affected / exposed      | 0 / 9 (0.00%)  | 0 / 21 (0.00%)  | 0 / 20 (0.00%)  |
| occurrences (all)                | 0              | 0               | 0               |
| Dysphagia                        |                |                 |                 |
| subjects affected / exposed      | 1 / 9 (11.11%) | 0 / 21 (0.00%)  | 2 / 20 (10.00%) |
| occurrences (all)                | 1              | 0               | 2               |
| Flatulence                       |                |                 |                 |
| subjects affected / exposed      | 0 / 9 (0.00%)  | 3 / 21 (14.29%) | 0 / 20 (0.00%)  |
| occurrences (all)                | 0              | 3               | 0               |
| Gastritis                        |                |                 |                 |
| subjects affected / exposed      | 1 / 9 (11.11%) | 1 / 21 (4.76%)  | 0 / 20 (0.00%)  |
| occurrences (all)                | 1              | 1               | 0               |
| Gastritis erosive                |                |                 |                 |
| subjects affected / exposed      | 0 / 9 (0.00%)  | 0 / 21 (0.00%)  | 0 / 20 (0.00%)  |
| occurrences (all)                | 0              | 0               | 0               |
| Gastrointestinal disorder        |                |                 |                 |
| subjects affected / exposed      | 0 / 9 (0.00%)  | 0 / 21 (0.00%)  | 0 / 20 (0.00%)  |
| occurrences (all)                | 0              | 0               | 0               |
| Gastrooesophageal reflux disease |                |                 |                 |
| subjects affected / exposed      | 0 / 9 (0.00%)  | 0 / 21 (0.00%)  | 1 / 20 (5.00%)  |
| occurrences (all)                | 0              | 0               | 1               |
| Haemorrhoids                     |                |                 |                 |
| subjects affected / exposed      | 0 / 9 (0.00%)  | 0 / 21 (0.00%)  | 0 / 20 (0.00%)  |
| occurrences (all)                | 0              | 0               | 0               |

|                                    |                |                 |                 |
|------------------------------------|----------------|-----------------|-----------------|
| Lip dry                            |                |                 |                 |
| subjects affected / exposed        | 0 / 9 (0.00%)  | 0 / 21 (0.00%)  | 0 / 20 (0.00%)  |
| occurrences (all)                  | 0              | 0               | 0               |
| Melaena                            |                |                 |                 |
| subjects affected / exposed        | 0 / 9 (0.00%)  | 0 / 21 (0.00%)  | 0 / 20 (0.00%)  |
| occurrences (all)                  | 0              | 0               | 0               |
| Lower gastrointestinal haemorrhage |                |                 |                 |
| subjects affected / exposed        | 0 / 9 (0.00%)  | 0 / 21 (0.00%)  | 0 / 20 (0.00%)  |
| occurrences (all)                  | 0              | 0               | 0               |
| Nausea                             |                |                 |                 |
| subjects affected / exposed        | 1 / 9 (11.11%) | 4 / 21 (19.05%) | 4 / 20 (20.00%) |
| occurrences (all)                  | 1              | 5               | 4               |
| Odynophagia                        |                |                 |                 |
| subjects affected / exposed        | 0 / 9 (0.00%)  | 1 / 21 (4.76%)  | 0 / 20 (0.00%)  |
| occurrences (all)                  | 0              | 1               | 0               |
| Oral mucosal erythema              |                |                 |                 |
| subjects affected / exposed        | 0 / 9 (0.00%)  | 0 / 21 (0.00%)  | 0 / 20 (0.00%)  |
| occurrences (all)                  | 0              | 0               | 0               |
| Retching                           |                |                 |                 |
| subjects affected / exposed        | 0 / 9 (0.00%)  | 0 / 21 (0.00%)  | 0 / 20 (0.00%)  |
| occurrences (all)                  | 0              | 0               | 0               |
| Stomatitis                         |                |                 |                 |
| subjects affected / exposed        | 0 / 9 (0.00%)  | 2 / 21 (9.52%)  | 0 / 20 (0.00%)  |
| occurrences (all)                  | 0              | 2               | 0               |
| Subileus                           |                |                 |                 |
| subjects affected / exposed        | 0 / 9 (0.00%)  | 0 / 21 (0.00%)  | 0 / 20 (0.00%)  |
| occurrences (all)                  | 0              | 0               | 0               |
| Toothache                          |                |                 |                 |
| subjects affected / exposed        | 0 / 9 (0.00%)  | 0 / 21 (0.00%)  | 0 / 20 (0.00%)  |
| occurrences (all)                  | 0              | 0               | 0               |
| Vomiting                           |                |                 |                 |
| subjects affected / exposed        | 2 / 9 (22.22%) | 3 / 21 (14.29%) | 1 / 20 (5.00%)  |
| occurrences (all)                  | 3              | 3               | 1               |
| Hepatobiliary disorders            |                |                 |                 |
| Cholangitis                        |                |                 |                 |



|  |               |                |                 |
|--|---------------|----------------|-----------------|
| subjects affected / exposed            | 0 / 9 (0.00%) | 0 / 21 (0.00%) | 0 / 20 (0.00%)  |
| occurrences (all)                      | 0             | 0              | 0               |
| Hepatic cytolysis                      |               |                |                 |
| subjects affected / exposed            | 0 / 9 (0.00%) | 0 / 21 (0.00%) | 0 / 20 (0.00%)  |
| occurrences (all)                      | 0             | 0              | 0               |
| Hepatic pain                           |               |                |                 |
| subjects affected / exposed            | 0 / 9 (0.00%) | 0 / 21 (0.00%) | 0 / 20 (0.00%)  |
| occurrences (all)                      | 0             | 0              | 0               |
| Skin and subcutaneous tissue disorders |               |                |                 |
| Dermatitis psoriasiform                |               |                |                 |
| subjects affected / exposed            | 0 / 9 (0.00%) | 0 / 21 (0.00%) | 0 / 20 (0.00%)  |
| occurrences (all)                      | 0             | 0              | 0               |
| Dermatitis acneiform                   |               |                |                 |
| subjects affected / exposed            | 0 / 9 (0.00%) | 0 / 21 (0.00%) | 2 / 20 (10.00%) |
| occurrences (all)                      | 0             | 0              | 2               |
| Dry skin                               |               |                |                 |
| subjects affected / exposed            | 0 / 9 (0.00%) | 2 / 21 (9.52%) | 0 / 20 (0.00%)  |
| occurrences (all)                      | 0             | 2              | 0               |
| Intertrigo                             |               |                |                 |
| subjects affected / exposed            | 0 / 9 (0.00%) | 0 / 21 (0.00%) | 0 / 20 (0.00%)  |
| occurrences (all)                      | 0             | 0              | 0               |
| Macule                                 |               |                |                 |
| subjects affected / exposed            | 0 / 9 (0.00%) | 0 / 21 (0.00%) | 0 / 20 (0.00%)  |
| occurrences (all)                      | 0             | 0              | 0               |
| Night sweats                           |               |                |                 |
| subjects affected / exposed            | 0 / 9 (0.00%) | 0 / 21 (0.00%) | 2 / 20 (10.00%) |
| occurrences (all)                      | 0             | 0              | 3               |
| Eczema                                 |               |                |                 |
| subjects affected / exposed            | 0 / 9 (0.00%) | 0 / 21 (0.00%) | 0 / 20 (0.00%)  |
| occurrences (all)                      | 0             | 0              | 0               |
| Erythema                               |               |                |                 |
| subjects affected / exposed            | 0 / 9 (0.00%) | 0 / 21 (0.00%) | 0 / 20 (0.00%)  |
| occurrences (all)                      | 0             | 0              | 0               |
| Prurigo                                |               |                |                 |
| subjects affected / exposed            | 0 / 9 (0.00%) | 0 / 21 (0.00%) | 0 / 20 (0.00%)  |
| occurrences (all)                      | 0             | 0              | 0               |

|                             |                |                 |                 |
|-----------------------------|----------------|-----------------|-----------------|
| Pruritus                    |                |                 |                 |
| subjects affected / exposed | 0 / 9 (0.00%)  | 2 / 21 (9.52%)  | 1 / 20 (5.00%)  |
| occurrences (all)           | 0              | 3               | 1               |
| Psoriasis                   |                |                 |                 |
| subjects affected / exposed | 0 / 9 (0.00%)  | 0 / 21 (0.00%)  | 0 / 20 (0.00%)  |
| occurrences (all)           | 0              | 0               | 0               |
| Petechiae                   |                |                 |                 |
| subjects affected / exposed | 0 / 9 (0.00%)  | 0 / 21 (0.00%)  | 0 / 20 (0.00%)  |
| occurrences (all)           | 0              | 0               | 0               |
| Skin ulcer                  |                |                 |                 |
| subjects affected / exposed | 0 / 9 (0.00%)  | 0 / 21 (0.00%)  | 0 / 20 (0.00%)  |
| occurrences (all)           | 0              | 0               | 0               |
| Rash                        |                |                 |                 |
| subjects affected / exposed | 0 / 9 (0.00%)  | 1 / 21 (4.76%)  | 0 / 20 (0.00%)  |
| occurrences (all)           | 0              | 1               | 0               |
| Rash maculo-papular         |                |                 |                 |
| subjects affected / exposed | 1 / 9 (11.11%) | 3 / 21 (14.29%) | 2 / 20 (10.00%) |
| occurrences (all)           | 1              | 3               | 2               |
| Purpura                     |                |                 |                 |
| subjects affected / exposed | 0 / 9 (0.00%)  | 0 / 21 (0.00%)  | 1 / 20 (5.00%)  |
| occurrences (all)           | 0              | 0               | 1               |
| Urticaria                   |                |                 |                 |
| subjects affected / exposed | 0 / 9 (0.00%)  | 0 / 21 (0.00%)  | 0 / 20 (0.00%)  |
| occurrences (all)           | 0              | 0               | 0               |
| Renal and urinary disorders |                |                 |                 |
| Dysuria                     |                |                 |                 |
| subjects affected / exposed | 0 / 9 (0.00%)  | 1 / 21 (4.76%)  | 0 / 20 (0.00%)  |
| occurrences (all)           | 0              | 1               | 0               |
| Haematuria                  |                |                 |                 |
| subjects affected / exposed | 0 / 9 (0.00%)  | 0 / 21 (0.00%)  | 0 / 20 (0.00%)  |
| occurrences (all)           | 0              | 0               | 0               |
| Pollakiuria                 |                |                 |                 |
| subjects affected / exposed | 0 / 9 (0.00%)  | 0 / 21 (0.00%)  | 0 / 20 (0.00%)  |
| occurrences (all)           | 0              | 0               | 0               |
| Urinary tract pain          |                |                 |                 |

|   |                |                 |                 |
|---|----------------|-----------------|-----------------|
| subjects affected / exposed                     | 0 / 9 (0.00%)  | 0 / 21 (0.00%)  | 0 / 20 (0.00%)  |
| occurrences (all)                               | 0              | 0               | 0               |
| Urinary retention                               |                |                 |                 |
| subjects affected / exposed                     | 0 / 9 (0.00%)  | 0 / 21 (0.00%)  | 0 / 20 (0.00%)  |
| occurrences (all)                               | 0              | 0               | 0               |
| Renal failure                                   |                |                 |                 |
| subjects affected / exposed                     | 0 / 9 (0.00%)  | 0 / 21 (0.00%)  | 0 / 20 (0.00%)  |
| occurrences (all)                               | 0              | 0               | 0               |
| Endocrine disorders                             |                |                 |                 |
| Hyperthyroidism                                 |                |                 |                 |
| subjects affected / exposed                     | 0 / 9 (0.00%)  | 3 / 21 (14.29%) | 1 / 20 (5.00%)  |
| occurrences (all)                               | 0              | 3               | 1               |
| Musculoskeletal and connective tissue disorders |                |                 |                 |
| Arthralgia                                      |                |                 |                 |
| subjects affected / exposed                     | 1 / 9 (11.11%) | 4 / 21 (19.05%) | 2 / 20 (10.00%) |
| occurrences (all)                               | 1              | 4               | 2               |
| Back pain                                       |                |                 |                 |
| subjects affected / exposed                     | 0 / 9 (0.00%)  | 3 / 21 (14.29%) | 3 / 20 (15.00%) |
| occurrences (all)                               | 0              | 4               | 4               |
| Bone pain                                       |                |                 |                 |
| subjects affected / exposed                     | 0 / 9 (0.00%)  | 1 / 21 (4.76%)  | 0 / 20 (0.00%)  |
| occurrences (all)                               | 0              | 1               | 0               |
| Flank pain                                      |                |                 |                 |
| subjects affected / exposed                     | 0 / 9 (0.00%)  | 0 / 21 (0.00%)  | 0 / 20 (0.00%)  |
| occurrences (all)                               | 0              | 0               | 0               |
| Groin pain                                      |                |                 |                 |
| subjects affected / exposed                     | 0 / 9 (0.00%)  | 0 / 21 (0.00%)  | 0 / 20 (0.00%)  |
| occurrences (all)                               | 0              | 0               | 0               |
| Muscular weakness                               |                |                 |                 |
| subjects affected / exposed                     | 0 / 9 (0.00%)  | 1 / 21 (4.76%)  | 0 / 20 (0.00%)  |
| occurrences (all)                               | 0              | 1               | 0               |
| Muscle spasms                                   |                |                 |                 |
| subjects affected / exposed                     | 1 / 9 (11.11%) | 0 / 21 (0.00%)  | 0 / 20 (0.00%)  |
| occurrences (all)                               | 1              | 0               | 0               |
| Myalgia   |                |                 |                 |

|                               |                |                |                |
|-------------------------------|----------------|----------------|----------------|
| subjects affected / exposed   | 0 / 9 (0.00%)  | 1 / 21 (4.76%) | 1 / 20 (5.00%) |
| occurrences (all)             | 0              | 1              | 1              |
| Neck pain                     |                |                |                |
| subjects affected / exposed   | 0 / 9 (0.00%)  | 0 / 21 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all)             | 0              | 0              | 1              |
| Pain in extremity             |                |                |                |
| subjects affected / exposed   | 0 / 9 (0.00%)  | 1 / 21 (4.76%) | 0 / 20 (0.00%) |
| occurrences (all)             | 0              | 1              | 0              |
| Pubic pain                    |                |                |                |
| subjects affected / exposed   | 0 / 9 (0.00%)  | 0 / 21 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all)             | 0              | 0              | 0              |
| Infections and infestations   |                |                |                |
| Bronchitis                    |                |                |                |
| subjects affected / exposed   | 1 / 9 (11.11%) | 0 / 21 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all)             | 1              | 0              | 0              |
| Bronchitis viral              |                |                |                |
| subjects affected / exposed   | 0 / 9 (0.00%)  | 0 / 21 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all)             | 0              | 0              | 0              |
| Clostridial infection         |                |                |                |
| subjects affected / exposed   | 0 / 9 (0.00%)  | 0 / 21 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all)             | 0              | 0              | 0              |
| Clostridium difficile colitis |                |                |                |
| subjects affected / exposed   | 0 / 9 (0.00%)  | 0 / 21 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all)             | 0              | 0              | 0              |
| Conjunctivitis                |                |                |                |
| subjects affected / exposed   | 0 / 9 (0.00%)  | 0 / 21 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all)             | 0              | 0              | 0              |
| Erysipelas                    |                |                |                |
| subjects affected / exposed   | 0 / 9 (0.00%)  | 0 / 21 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all)             | 0              | 0              | 0              |
| Diverticulitis                |                |                |                |
| subjects affected / exposed   | 0 / 9 (0.00%)  | 1 / 21 (4.76%) | 0 / 20 (0.00%) |
| occurrences (all)             | 0              | 1              | 0              |
| Cystitis                      |                |                |                |
| subjects affected / exposed   | 0 / 9 (0.00%)  | 0 / 21 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all)             | 0              | 0              | 0              |

|                                     |                |                |                |
|-------------------------------------|----------------|----------------|----------------|
| Gastroenteritis                     |                |                |                |
| subjects affected / exposed         | 1 / 9 (11.11%) | 0 / 21 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all)                   | 1              | 0              | 0              |
| Folliculitis                        |                |                |                |
| subjects affected / exposed         | 0 / 9 (0.00%)  | 0 / 21 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all)                   | 0              | 0              | 0              |
| Escherichia urinary tract infection |                |                |                |
| subjects affected / exposed         | 0 / 9 (0.00%)  | 0 / 21 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all)                   | 0              | 0              | 0              |
| Genital herpes simplex              |                |                |                |
| subjects affected / exposed         | 0 / 9 (0.00%)  | 0 / 21 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all)                   | 0              | 0              | 0              |
| Genital infection fungal            |                |                |                |
| subjects affected / exposed         | 1 / 9 (11.11%) | 0 / 21 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all)                   | 1              | 0              | 0              |
| Herpes dermatitis                   |                |                |                |
| subjects affected / exposed         | 0 / 9 (0.00%)  | 0 / 21 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all)                   | 0              | 0              | 0              |
| Impetigo                            |                |                |                |
| subjects affected / exposed         | 0 / 9 (0.00%)  | 0 / 21 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all)                   | 0              | 0              | 0              |
| Herpes zoster                       |                |                |                |
| subjects affected / exposed         | 0 / 9 (0.00%)  | 1 / 21 (4.76%) | 0 / 20 (0.00%) |
| occurrences (all)                   | 0              | 1              | 0              |
| Influenza                           |                |                |                |
| subjects affected / exposed         | 0 / 9 (0.00%)  | 0 / 21 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all)                   | 0              | 0              | 0              |
| Infection                           |                |                |                |
| subjects affected / exposed         | 0 / 9 (0.00%)  | 0 / 21 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all)                   | 0              | 0              | 1              |
| Nasopharyngitis                     |                |                |                |
| subjects affected / exposed         | 0 / 9 (0.00%)  | 0 / 21 (0.00%) | 1 / 20 (5.00%) |
| occurrences (all)                   | 0              | 0              | 1              |
| Oesophageal infection               |                |                |                |
| subjects affected / exposed         | 0 / 9 (0.00%)  | 0 / 21 (0.00%) | 0 / 20 (0.00%) |
| occurrences (all)                   | 0              | 0              | 0              |

|                                       |               |                |                 |
|---------------------------------------|---------------|----------------|-----------------|
| Pharyngitis                           |               |                |                 |
| subjects affected / exposed           | 0 / 9 (0.00%) | 0 / 21 (0.00%) | 0 / 20 (0.00%)  |
| occurrences (all)                     | 0             | 0              | 0               |
| Oral herpes                           |               |                |                 |
| subjects affected / exposed           | 0 / 9 (0.00%) | 0 / 21 (0.00%) | 1 / 20 (5.00%)  |
| occurrences (all)                     | 0             | 0              | 2               |
| Pneumonia                             |               |                |                 |
| subjects affected / exposed           | 0 / 9 (0.00%) | 0 / 21 (0.00%) | 2 / 20 (10.00%) |
| occurrences (all)                     | 0             | 0              | 2               |
| Rash pustular                         |               |                |                 |
| subjects affected / exposed           | 0 / 9 (0.00%) | 2 / 21 (9.52%) | 0 / 20 (0.00%)  |
| occurrences (all)                     | 0             | 2              | 0               |
| Respiratory tract infection           |               |                |                 |
| subjects affected / exposed           | 0 / 9 (0.00%) | 0 / 21 (0.00%) | 0 / 20 (0.00%)  |
| occurrences (all)                     | 0             | 0              | 0               |
| Respiratory tract infection bacterial |               |                |                 |
| subjects affected / exposed           | 0 / 9 (0.00%) | 0 / 21 (0.00%) | 0 / 20 (0.00%)  |
| occurrences (all)                     | 0             | 0              | 0               |
| Sinusitis                             |               |                |                 |
| subjects affected / exposed           | 0 / 9 (0.00%) | 1 / 21 (4.76%) | 0 / 20 (0.00%)  |
| occurrences (all)                     | 0             | 1              | 0               |
| Tooth abscess                         |               |                |                 |
| subjects affected / exposed           | 0 / 9 (0.00%) | 0 / 21 (0.00%) | 0 / 20 (0.00%)  |
| occurrences (all)                     | 0             | 0              | 0               |
| Tooth infection                       |               |                |                 |
| subjects affected / exposed           | 0 / 9 (0.00%) | 0 / 21 (0.00%) | 0 / 20 (0.00%)  |
| occurrences (all)                     | 0             | 0              | 0               |
| Tracheitis                            |               |                |                 |
| subjects affected / exposed           | 0 / 9 (0.00%) | 0 / 21 (0.00%) | 0 / 20 (0.00%)  |
| occurrences (all)                     | 0             | 0              | 0               |
| Upper respiratory tract infection     |               |                |                 |
| subjects affected / exposed           | 0 / 9 (0.00%) | 1 / 21 (4.76%) | 0 / 20 (0.00%)  |
| occurrences (all)                     | 0             | 1              | 0               |
| Urinary tract infection enterococcal  |               |                |                 |
| subjects affected / exposed           | 0 / 9 (0.00%) | 0 / 21 (0.00%) | 0 / 20 (0.00%)  |
| occurrences (all)                     | 0             | 0              | 0               |

|                                    |                |                 |                 |
|------------------------------------|----------------|-----------------|-----------------|
| Urinary tract infection            |                |                 |                 |
| subjects affected / exposed        | 0 / 9 (0.00%)  | 0 / 21 (0.00%)  | 0 / 20 (0.00%)  |
| occurrences (all)                  | 0              | 0               | 0               |
| Mucosal infection                  |                |                 |                 |
| subjects affected / exposed        | 0 / 9 (0.00%)  | 0 / 21 (0.00%)  | 0 / 20 (0.00%)  |
| occurrences (all)                  | 0              | 0               | 0               |
| Stoma site infection               |                |                 |                 |
| subjects affected / exposed        | 0 / 9 (0.00%)  | 0 / 21 (0.00%)  | 0 / 20 (0.00%)  |
| occurrences (all)                  | 0              | 0               | 0               |
| Metabolism and nutrition disorders |                |                 |                 |
| Acidosis                           |                |                 |                 |
| subjects affected / exposed        | 1 / 9 (11.11%) | 0 / 21 (0.00%)  | 0 / 20 (0.00%)  |
| occurrences (all)                  | 1              | 0               | 0               |
| Decreased appetite                 |                |                 |                 |
| subjects affected / exposed        | 2 / 9 (22.22%) | 3 / 21 (14.29%) | 5 / 20 (25.00%) |
| occurrences (all)                  | 4              | 3               | 5               |
| Cell death                         |                |                 |                 |
| subjects affected / exposed        | 0 / 9 (0.00%)  | 0 / 21 (0.00%)  | 0 / 20 (0.00%)  |
| occurrences (all)                  | 0              | 0               | 0               |
| Dehydration                        |                |                 |                 |
| subjects affected / exposed        | 0 / 9 (0.00%)  | 0 / 21 (0.00%)  | 0 / 20 (0.00%)  |
| occurrences (all)                  | 0              | 0               | 0               |
| Fluid retention                    |                |                 |                 |
| subjects affected / exposed        | 0 / 9 (0.00%)  | 0 / 21 (0.00%)  | 0 / 20 (0.00%)  |
| occurrences (all)                  | 0              | 0               | 0               |
| Folate deficiency                  |                |                 |                 |
| subjects affected / exposed        | 0 / 9 (0.00%)  | 0 / 21 (0.00%)  | 0 / 20 (0.00%)  |
| occurrences (all)                  | 0              | 0               | 0               |
| Gout                               |                |                 |                 |
| subjects affected / exposed        | 1 / 9 (11.11%) | 0 / 21 (0.00%)  | 0 / 20 (0.00%)  |
| occurrences (all)                  | 1              | 0               | 0               |
| Hypercalcaemia                     |                |                 |                 |
| subjects affected / exposed        | 0 / 9 (0.00%)  | 4 / 21 (19.05%) | 2 / 20 (10.00%) |
| occurrences (all)                  | 0              | 4               | 3               |
| Hyperkalaemia                      |                |                 |                 |

|                             |                |                 |                 |
|-----------------------------|----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 9 (0.00%)  | 1 / 21 (4.76%)  | 0 / 20 (0.00%)  |
| occurrences (all)           | 0              | 1               | 0               |
| Hyperglycaemia              |                |                 |                 |
| subjects affected / exposed | 0 / 9 (0.00%)  | 0 / 21 (0.00%)  | 4 / 20 (20.00%) |
| occurrences (all)           | 0              | 0               | 6               |
| Hyperphosphataemia          |                |                 |                 |
| subjects affected / exposed | 0 / 9 (0.00%)  | 1 / 21 (4.76%)  | 2 / 20 (10.00%) |
| occurrences (all)           | 0              | 2               | 4               |
| Hypoalbuminaemia            |                |                 |                 |
| subjects affected / exposed | 0 / 9 (0.00%)  | 1 / 21 (4.76%)  | 4 / 20 (20.00%) |
| occurrences (all)           | 0              | 2               | 11              |
| Hypocalcaemia               |                |                 |                 |
| subjects affected / exposed | 0 / 9 (0.00%)  | 0 / 21 (0.00%)  | 2 / 20 (10.00%) |
| occurrences (all)           | 0              | 0               | 5               |
| Hypokalaemia                |                |                 |                 |
| subjects affected / exposed | 0 / 9 (0.00%)  | 4 / 21 (19.05%) | 3 / 20 (15.00%) |
| occurrences (all)           | 0              | 7               | 5               |
| Hypomagnesaemia             |                |                 |                 |
| subjects affected / exposed | 0 / 9 (0.00%)  | 1 / 21 (4.76%)  | 4 / 20 (20.00%) |
| occurrences (all)           | 0              | 1               | 4               |
| Hyponatraemia               |                |                 |                 |
| subjects affected / exposed | 1 / 9 (11.11%) | 5 / 21 (23.81%) | 8 / 20 (40.00%) |
| occurrences (all)           | 1              | 7               | 15              |
| Hypophosphataemia           |                |                 |                 |
| subjects affected / exposed | 0 / 9 (0.00%)  | 1 / 21 (4.76%)  | 3 / 20 (15.00%) |
| occurrences (all)           | 0              | 1               | 4               |
| Malnutrition                |                |                 |                 |
| subjects affected / exposed | 0 / 9 (0.00%)  | 0 / 21 (0.00%)  | 0 / 20 (0.00%)  |
| occurrences (all)           | 0              | 0               | 0               |

| <b>Non-serious adverse events</b>                                   | Phase Ib - Schedule B: 2 mg BI 894999 (mCRPC patients) | Phase Ib - Schedule B: 2.5 mg BI 894999 (mCRPC patients) | Phase Ib - Schedule B: 2.5 mg BI 894999 (CRC patients) |
|---|--|--|--|
| Total subjects affected by non-serious adverse events               |  |  |  |
| subjects affected / exposed   | 1 / 1 (100.00%)  | 10 / 10 (100.00%)  | 14 / 14 (100.00%)                                      |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |  |  |  |



|   |                      |                      |                      |
|---|----------------------|----------------------|----------------------|
| Tumour pain<br>subjects affected / exposed<br>occurrences (all)             | 0 / 1 (0.00%)<br>0   | 0 / 10 (0.00%)<br>0  | 0 / 14 (0.00%)<br>0  |
| Vascular disorders  |                      |                      |                      |
| Hypotension<br>subjects affected / exposed<br>occurrences (all)             | 0 / 1 (0.00%)<br>0   | 0 / 10 (0.00%)<br>0  | 1 / 14 (7.14%)<br>1  |
| Hypertension<br>subjects affected / exposed<br>occurrences (all)            | 0 / 1 (0.00%)<br>0   | 1 / 10 (10.00%)<br>2 | 1 / 14 (7.14%)<br>2  |
| Haematoma<br>subjects affected / exposed<br>occurrences (all)               | 1 / 1 (100.00%)<br>1 | 1 / 10 (10.00%)<br>1 | 2 / 14 (14.29%)<br>2 |
| Orthostatic hypotension<br>subjects affected / exposed<br>occurrences (all) | 0 / 1 (0.00%)<br>0   | 0 / 10 (0.00%)<br>0  | 0 / 14 (0.00%)<br>0  |
| Pallor<br>subjects affected / exposed<br>occurrences (all)                  | 0 / 1 (0.00%)<br>0   | 0 / 10 (0.00%)<br>0  | 0 / 14 (0.00%)<br>0  |
| General disorders and administration<br>site conditions                     |                      |                      |                      |
| Chest discomfort<br>subjects affected / exposed<br>occurrences (all)        | 0 / 1 (0.00%)<br>0   | 0 / 10 (0.00%)<br>0  | 0 / 14 (0.00%)<br>0  |
| Asthenia<br>subjects affected / exposed<br>occurrences (all)                | 0 / 1 (0.00%)<br>0   | 1 / 10 (10.00%)<br>1 | 2 / 14 (14.29%)<br>3 |
| Chest pain<br>subjects affected / exposed<br>occurrences (all)              | 0 / 1 (0.00%)<br>0   | 0 / 10 (0.00%)<br>0  | 1 / 14 (7.14%)<br>1  |
| Fatigue<br>subjects affected / exposed<br>occurrences (all)                 | 0 / 1 (0.00%)<br>0   | 6 / 10 (60.00%)<br>9 | 6 / 14 (42.86%)<br>8 |
| Facial pain<br>subjects affected / exposed<br>occurrences (all)             | 0 / 1 (0.00%)<br>0   | 0 / 10 (0.00%)<br>0  | 0 / 14 (0.00%)<br>0  |
| Chills  |                      |                      |                      |

|                                       |               |                 |                |
|---------------------------------------|---------------|-----------------|----------------|
| subjects affected / exposed           | 0 / 1 (0.00%) | 0 / 10 (0.00%)  | 0 / 14 (0.00%) |
| occurrences (all)                     | 0             | 0               | 0              |
| Gait disturbance                      |               |                 |                |
| subjects affected / exposed           | 0 / 1 (0.00%) | 0 / 10 (0.00%)  | 0 / 14 (0.00%) |
| occurrences (all)                     | 0             | 0               | 0              |
| General physical health deterioration |               |                 |                |
| subjects affected / exposed           | 0 / 1 (0.00%) | 0 / 10 (0.00%)  | 0 / 14 (0.00%) |
| occurrences (all)                     | 0             | 0               | 0              |
| Generalised oedema                    |               |                 |                |
| subjects affected / exposed           | 0 / 1 (0.00%) | 0 / 10 (0.00%)  | 1 / 14 (7.14%) |
| occurrences (all)                     | 0             | 0               | 1              |
| Malaise                               |               |                 |                |
| subjects affected / exposed           | 0 / 1 (0.00%) | 0 / 10 (0.00%)  | 1 / 14 (7.14%) |
| occurrences (all)                     | 0             | 0               | 1              |
| Hypothermia                           |               |                 |                |
| subjects affected / exposed           | 0 / 1 (0.00%) | 0 / 10 (0.00%)  | 0 / 14 (0.00%) |
| occurrences (all)                     | 0             | 0               | 0              |
| Oedema peripheral                     |               |                 |                |
| subjects affected / exposed           | 0 / 1 (0.00%) | 3 / 10 (30.00%) | 1 / 14 (7.14%) |
| occurrences (all)                     | 0             | 5               | 1              |
| Non-cardiac chest pain                |               |                 |                |
| subjects affected / exposed           | 0 / 1 (0.00%) | 1 / 10 (10.00%) | 0 / 14 (0.00%) |
| occurrences (all)                     | 0             | 1               | 0              |
| Pain                                  |               |                 |                |
| subjects affected / exposed           | 0 / 1 (0.00%) | 0 / 10 (0.00%)  | 0 / 14 (0.00%) |
| occurrences (all)                     | 0             | 0               | 0              |
| Pyrexia                               |               |                 |                |
| subjects affected / exposed           | 0 / 1 (0.00%) | 1 / 10 (10.00%) | 0 / 14 (0.00%) |
| occurrences (all)                     | 0             | 1               | 0              |
| Peripheral swelling                   |               |                 |                |
| subjects affected / exposed           | 0 / 1 (0.00%) | 1 / 10 (10.00%) | 0 / 14 (0.00%) |
| occurrences (all)                     | 0             | 1               | 0              |
| Immune system disorders               |               |                 |                |
| Hypersensitivity                      |               |                 |                |
| subjects affected / exposed           | 0 / 1 (0.00%) | 0 / 10 (0.00%)  | 0 / 14 (0.00%) |
| occurrences (all)                     | 0             | 0               | 0              |

|  |                    |                      |                     |
|--|--------------------|----------------------|---------------------|
| Iodine allergy<br>subjects affected / exposed<br>occurrences (all)           | 0 / 1 (0.00%)<br>0 | 0 / 10 (0.00%)<br>0  | 0 / 14 (0.00%)<br>0 |
| Reproductive system and breast disorders                                     |                    |                      |                     |
| Erectile dysfunction<br>subjects affected / exposed<br>occurrences (all)     | 0 / 1 (0.00%)<br>0 | 0 / 10 (0.00%)<br>0  | 0 / 14 (0.00%)<br>0 |
| Heavy menstrual bleeding<br>subjects affected / exposed<br>occurrences (all) | 0 / 1 (0.00%)<br>0 | 0 / 10 (0.00%)<br>0  | 0 / 14 (0.00%)<br>0 |
| Oedema genital<br>subjects affected / exposed<br>occurrences (all)           | 0 / 1 (0.00%)<br>0 | 0 / 10 (0.00%)<br>0  | 0 / 14 (0.00%)<br>0 |
| Perineal pain<br>subjects affected / exposed<br>occurrences (all)            | 0 / 1 (0.00%)<br>0 | 0 / 10 (0.00%)<br>0  | 0 / 14 (0.00%)<br>0 |
| Scrotal oedema<br>subjects affected / exposed<br>occurrences (all)           | 0 / 1 (0.00%)<br>0 | 0 / 10 (0.00%)<br>0  | 0 / 14 (0.00%)<br>0 |
| Testicular pain<br>subjects affected / exposed<br>occurrences (all)          | 0 / 1 (0.00%)<br>0 | 0 / 10 (0.00%)<br>0  | 0 / 14 (0.00%)<br>0 |
| Vulvovaginal discomfort<br>subjects affected / exposed<br>occurrences (all)  | 0 / 1 (0.00%)<br>0 | 0 / 10 (0.00%)<br>0  | 0 / 14 (0.00%)<br>0 |
| Vaginal haemorrhage<br>subjects affected / exposed<br>occurrences (all)      | 0 / 1 (0.00%)<br>0 | 0 / 10 (0.00%)<br>0  | 0 / 14 (0.00%)<br>0 |
| Respiratory, thoracic and mediastinal disorders                              |                    |                      |                     |
| Atelectasis<br>subjects affected / exposed<br>occurrences (all)              | 0 / 1 (0.00%)<br>0 | 0 / 10 (0.00%)<br>0  | 0 / 14 (0.00%)<br>0 |
| Dysphonia<br>subjects affected / exposed<br>occurrences (all)                | 0 / 1 (0.00%)<br>0 | 1 / 10 (10.00%)<br>1 | 0 / 14 (0.00%)<br>0 |
| Cough  |                    |                      |                     |

|                             |                 |                 |                 |
|-----------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 1 (0.00%)   | 1 / 10 (10.00%) | 3 / 14 (21.43%) |
| occurrences (all)           | 0               | 1               | 3               |
| Dyspnoea                    |                 |                 |                 |
| subjects affected / exposed | 0 / 1 (0.00%)   | 4 / 10 (40.00%) | 3 / 14 (21.43%) |
| occurrences (all)           | 0               | 6               | 5               |
| Dyspnoea exertional         |                 |                 |                 |
| subjects affected / exposed | 0 / 1 (0.00%)   | 0 / 10 (0.00%)  | 0 / 14 (0.00%)  |
| occurrences (all)           | 0               | 0               | 0               |
| Epistaxis                   |                 |                 |                 |
| subjects affected / exposed | 1 / 1 (100.00%) | 2 / 10 (20.00%) | 1 / 14 (7.14%)  |
| occurrences (all)           | 1               | 2               | 1               |
| Laryngeal inflammation      |                 |                 |                 |
| subjects affected / exposed | 0 / 1 (0.00%)   | 0 / 10 (0.00%)  | 0 / 14 (0.00%)  |
| occurrences (all)           | 0               | 0               | 0               |
| Haemoptysis                 |                 |                 |                 |
| subjects affected / exposed | 0 / 1 (0.00%)   | 0 / 10 (0.00%)  | 0 / 14 (0.00%)  |
| occurrences (all)           | 0               | 0               | 0               |
| Nasal discomfort            |                 |                 |                 |
| subjects affected / exposed | 0 / 1 (0.00%)   | 0 / 10 (0.00%)  | 0 / 14 (0.00%)  |
| occurrences (all)           | 0               | 0               | 0               |
| Oropharyngeal pain          |                 |                 |                 |
| subjects affected / exposed | 0 / 1 (0.00%)   | 0 / 10 (0.00%)  | 0 / 14 (0.00%)  |
| occurrences (all)           | 0               | 0               | 0               |
| Pharyngeal inflammation     |                 |                 |                 |
| subjects affected / exposed | 0 / 1 (0.00%)   | 1 / 10 (10.00%) | 0 / 14 (0.00%)  |
| occurrences (all)           | 0               | 1               | 0               |
| Pleural effusion            |                 |                 |                 |
| subjects affected / exposed | 0 / 1 (0.00%)   | 0 / 10 (0.00%)  | 0 / 14 (0.00%)  |
| occurrences (all)           | 0               | 0               | 0               |
| Pleuritic pain              |                 |                 |                 |
| subjects affected / exposed | 0 / 1 (0.00%)   | 0 / 10 (0.00%)  | 0 / 14 (0.00%)  |
| occurrences (all)           | 0               | 0               | 0               |
| Productive cough            |                 |                 |                 |
| subjects affected / exposed | 0 / 1 (0.00%)   | 1 / 10 (10.00%) | 0 / 14 (0.00%)  |
| occurrences (all)           | 0               | 1               | 0               |
| Rhinorrhoea                 |                 |                 |                 |

|  |                    |                      |                     |
|--|--------------------|----------------------|---------------------|
| subjects affected / exposed<br>occurrences (all)                                 | 0 / 1 (0.00%)<br>0 | 0 / 10 (0.00%)<br>0  | 0 / 14 (0.00%)<br>0 |
| Respiratory tract congestion<br>subjects affected / exposed<br>occurrences (all) | 0 / 1 (0.00%)<br>0 | 0 / 10 (0.00%)<br>0  | 0 / 14 (0.00%)<br>0 |
| Wheezing<br>subjects affected / exposed<br>occurrences (all)                     | 0 / 1 (0.00%)<br>0 | 1 / 10 (10.00%)<br>1 | 1 / 14 (7.14%)<br>1 |
| Psychiatric disorders  |                    |                      |                     |
| Affective disorder<br>subjects affected / exposed<br>occurrences (all)           | 0 / 1 (0.00%)<br>0 | 0 / 10 (0.00%)<br>0  | 1 / 14 (7.14%)<br>1 |
| Agitation<br>subjects affected / exposed<br>occurrences (all)                    | 0 / 1 (0.00%)<br>0 | 0 / 10 (0.00%)<br>0  | 0 / 14 (0.00%)<br>0 |
| Anxiety<br>subjects affected / exposed<br>occurrences (all)                      | 0 / 1 (0.00%)<br>0 | 0 / 10 (0.00%)<br>0  | 1 / 14 (7.14%)<br>1 |
| Confusional state<br>subjects affected / exposed<br>occurrences (all)            | 0 / 1 (0.00%)<br>0 | 2 / 10 (20.00%)<br>2 | 1 / 14 (7.14%)<br>1 |
| Depression<br>subjects affected / exposed<br>occurrences (all)                   | 0 / 1 (0.00%)<br>0 | 1 / 10 (10.00%)<br>1 | 0 / 14 (0.00%)<br>0 |
| Insomnia<br>subjects affected / exposed<br>occurrences (all)                     | 0 / 1 (0.00%)<br>0 | 0 / 10 (0.00%)<br>0  | 0 / 14 (0.00%)<br>0 |
| Hallucination<br>subjects affected / exposed<br>occurrences (all)                | 0 / 1 (0.00%)<br>0 | 0 / 10 (0.00%)<br>0  | 0 / 14 (0.00%)<br>0 |
| Personality change<br>subjects affected / exposed<br>occurrences (all)           | 0 / 1 (0.00%)<br>0 | 0 / 10 (0.00%)<br>0  | 0 / 14 (0.00%)<br>0 |
| Sleep disorder<br>subjects affected / exposed<br>occurrences (all)               | 0 / 1 (0.00%)<br>0 | 0 / 10 (0.00%)<br>0  | 0 / 14 (0.00%)<br>0 |

|   |                 |                |                 |
|---|-----------------|----------------|-----------------|
| Investigations                                  |                 |                |                 |
| Activated partial thromboplastin time prolonged |                 |                |                 |
| subjects affected / exposed                     | 0 / 1 (0.00%)   | 0 / 10 (0.00%) | 1 / 14 (7.14%)  |
| occurrences (all)                               | 0               | 0              | 1               |
| Activated partial thromboplastin time shortened |                 |                |                 |
| subjects affected / exposed                     | 0 / 1 (0.00%)   | 0 / 10 (0.00%) | 0 / 14 (0.00%)  |
| occurrences (all)                               | 0               | 0              | 0               |
| Alanine aminotransferase increased              |                 |                |                 |
| subjects affected / exposed                     | 0 / 1 (0.00%)   | 0 / 10 (0.00%) | 1 / 14 (7.14%)  |
| occurrences (all)                               | 0               | 0              | 1               |
| Aspartate aminotransferase increased            |                 |                |                 |
| subjects affected / exposed                     | 1 / 1 (100.00%) | 0 / 10 (0.00%) | 1 / 14 (7.14%)  |
| occurrences (all)                               | 1               | 0              | 1               |
| Blood alkaline phosphatase increased            |                 |                |                 |
| subjects affected / exposed                     | 0 / 1 (0.00%)   | 0 / 10 (0.00%) | 1 / 14 (7.14%)  |
| occurrences (all)                               | 0               | 0              | 2               |
| Blood antidiuretic hormone decreased            |                 |                |                 |
| subjects affected / exposed                     | 0 / 1 (0.00%)   | 0 / 10 (0.00%) | 0 / 14 (0.00%)  |
| occurrences (all)                               | 0               | 0              | 0               |
| Blood bilirubin increased                       |                 |                |                 |
| subjects affected / exposed                     | 0 / 1 (0.00%)   | 0 / 10 (0.00%) | 2 / 14 (14.29%) |
| occurrences (all)                               | 0               | 0              | 2               |
| Blood creatine phosphokinase increased          |                 |                |                 |
| subjects affected / exposed                     | 0 / 1 (0.00%)   | 0 / 10 (0.00%) | 0 / 14 (0.00%)  |
| occurrences (all)                               | 0               | 0              | 0               |
| Blood creatinine increased                      |                 |                |                 |
| subjects affected / exposed                     | 0 / 1 (0.00%)   | 0 / 10 (0.00%) | 1 / 14 (7.14%)  |
| occurrences (all)                               | 0               | 0              | 2               |
| Blood magnesium decreased                       |                 |                |                 |
| subjects affected / exposed                     | 0 / 1 (0.00%)   | 0 / 10 (0.00%) | 0 / 14 (0.00%)  |
| occurrences (all)                               | 0               | 0              | 0               |
| Blood glucose increased                         |                 |                |                 |
| subjects affected / exposed                     | 0 / 1 (0.00%)   | 0 / 10 (0.00%) | 0 / 14 (0.00%)  |
| occurrences (all)                               | 0               | 0              | 0               |

|   |                    |                     |                     |
|---|--------------------|---------------------|---------------------|
| C-reactive protein increased<br>subjects affected / exposed<br>occurrences (all)                | 0 / 1 (0.00%)<br>0 | 0 / 10 (0.00%)<br>0 | 0 / 14 (0.00%)<br>0 |
| Cardiac murmur<br>subjects affected / exposed<br>occurrences (all)                              | 0 / 1 (0.00%)<br>0 | 0 / 10 (0.00%)<br>0 | 0 / 14 (0.00%)<br>0 |
| Cortisol increased<br>subjects affected / exposed<br>occurrences (all)                          | 0 / 1 (0.00%)<br>0 | 0 / 10 (0.00%)<br>0 | 0 / 14 (0.00%)<br>0 |
| Echocardiogram abnormal<br>subjects affected / exposed<br>occurrences (all)                     | 0 / 1 (0.00%)<br>0 | 0 / 10 (0.00%)<br>0 | 0 / 14 (0.00%)<br>0 |
| Electrocardiogram PR prolongation<br>subjects affected / exposed<br>occurrences (all)           | 0 / 1 (0.00%)<br>0 | 0 / 10 (0.00%)<br>0 | 0 / 14 (0.00%)<br>0 |
| Ejection fraction decreased<br>subjects affected / exposed<br>occurrences (all)                 | 0 / 1 (0.00%)<br>0 | 0 / 10 (0.00%)<br>0 | 0 / 14 (0.00%)<br>0 |
| Electrocardiogram ST segment<br>elevation<br>subjects affected / exposed<br>occurrences (all)   | 0 / 1 (0.00%)<br>0 | 0 / 10 (0.00%)<br>0 | 0 / 14 (0.00%)<br>0 |
| Gamma-glutamyltransferase<br>increased<br>subjects affected / exposed<br>occurrences (all)      | 0 / 1 (0.00%)<br>0 | 0 / 10 (0.00%)<br>0 | 0 / 14 (0.00%)<br>0 |
| Electrocardiogram T wave inversion<br>subjects affected / exposed<br>occurrences (all)          | 0 / 1 (0.00%)<br>0 | 0 / 10 (0.00%)<br>0 | 0 / 14 (0.00%)<br>0 |
| International normalised ratio<br>increased<br>subjects affected / exposed<br>occurrences (all) | 0 / 1 (0.00%)<br>0 | 0 / 10 (0.00%)<br>0 | 0 / 14 (0.00%)<br>0 |
| Lymphocyte count decreased<br>subjects affected / exposed<br>occurrences (all)                  | 0 / 1 (0.00%)<br>0 | 0 / 10 (0.00%)<br>0 | 0 / 14 (0.00%)<br>0 |
| Neutrophil count decreased  |                    |                     |                     |

|  |                      |                      |                     |
|--|----------------------|----------------------|---------------------|
| subjects affected / exposed<br>occurrences (all)                                     | 0 / 1 (0.00%)<br>0   | 0 / 10 (0.00%)<br>0  | 0 / 14 (0.00%)<br>0 |
| Platelet count decreased<br>subjects affected / exposed<br>occurrences (all)         | 1 / 1 (100.00%)<br>1 | 2 / 10 (20.00%)<br>2 | 1 / 14 (7.14%)<br>1 |
| Prothrombin level decreased<br>subjects affected / exposed<br>occurrences (all)      | 0 / 1 (0.00%)<br>0   | 0 / 10 (0.00%)<br>0  | 0 / 14 (0.00%)<br>0 |
| Troponin I increased<br>subjects affected / exposed<br>occurrences (all)             | 0 / 1 (0.00%)<br>0   | 0 / 10 (0.00%)<br>0  | 0 / 14 (0.00%)<br>0 |
| Troponin T increased<br>subjects affected / exposed<br>occurrences (all)             | 0 / 1 (0.00%)<br>0   | 1 / 10 (10.00%)<br>1 | 0 / 14 (0.00%)<br>0 |
| Troponin increased<br>subjects affected / exposed<br>occurrences (all)               | 0 / 1 (0.00%)<br>0   | 1 / 10 (10.00%)<br>1 | 1 / 14 (7.14%)<br>1 |
| Urine output decreased<br>subjects affected / exposed<br>occurrences (all)           | 0 / 1 (0.00%)<br>0   | 0 / 10 (0.00%)<br>0  | 0 / 14 (0.00%)<br>0 |
| Weight decreased<br>subjects affected / exposed<br>occurrences (all)                 | 0 / 1 (0.00%)<br>0   | 4 / 10 (40.00%)<br>5 | 1 / 14 (7.14%)<br>1 |
| White blood cell count decreased<br>subjects affected / exposed<br>occurrences (all) | 0 / 1 (0.00%)<br>0   | 0 / 10 (0.00%)<br>0  | 0 / 14 (0.00%)<br>0 |
| Injury, poisoning and procedural complications                                       |                      |                      |                     |
| Contusion<br>subjects affected / exposed<br>occurrences (all)                        | 0 / 1 (0.00%)<br>0   | 0 / 10 (0.00%)<br>0  | 0 / 14 (0.00%)<br>0 |
| Face injury<br>subjects affected / exposed<br>occurrences (all)                      | 0 / 1 (0.00%)<br>0   | 0 / 10 (0.00%)<br>0  | 0 / 14 (0.00%)<br>0 |
| Infusion related reaction  |                      |                      |                     |



|                                  |               |                 |                |
|----------------------------------|---------------|-----------------|----------------|
| subjects affected / exposed      | 0 / 1 (0.00%) | 1 / 10 (10.00%) | 0 / 14 (0.00%) |
| occurrences (all)                | 0             | 1               | 0              |
| Limb injury                      |               |                 |                |
| subjects affected / exposed      | 0 / 1 (0.00%) | 0 / 10 (0.00%)  | 0 / 14 (0.00%) |
| occurrences (all)                | 0             | 0               | 0              |
| Muscle rupture                   |               |                 |                |
| subjects affected / exposed      | 0 / 1 (0.00%) | 0 / 10 (0.00%)  | 0 / 14 (0.00%) |
| occurrences (all)                | 0             | 0               | 0              |
| Overdose                         |               |                 |                |
| subjects affected / exposed      | 0 / 1 (0.00%) | 0 / 10 (0.00%)  | 0 / 14 (0.00%) |
| occurrences (all)                | 0             | 0               | 0              |
| Post procedural haematoma        |               |                 |                |
| subjects affected / exposed      | 0 / 1 (0.00%) | 0 / 10 (0.00%)  | 0 / 14 (0.00%) |
| occurrences (all)                | 0             | 0               | 0              |
| Skin abrasion                    |               |                 |                |
| subjects affected / exposed      | 0 / 1 (0.00%) | 0 / 10 (0.00%)  | 0 / 14 (0.00%) |
| occurrences (all)                | 0             | 0               | 0              |
| Procedural pain                  |               |                 |                |
| subjects affected / exposed      | 0 / 1 (0.00%) | 0 / 10 (0.00%)  | 1 / 14 (7.14%) |
| occurrences (all)                | 0             | 0               | 1              |
| Subcutaneous haematoma           |               |                 |                |
| subjects affected / exposed      | 0 / 1 (0.00%) | 0 / 10 (0.00%)  | 0 / 14 (0.00%) |
| occurrences (all)                | 0             | 0               | 0              |
| Skin laceration                  |               |                 |                |
| subjects affected / exposed      | 0 / 1 (0.00%) | 0 / 10 (0.00%)  | 0 / 14 (0.00%) |
| occurrences (all)                | 0             | 0               | 0              |
| Tongue injury                    |               |                 |                |
| subjects affected / exposed      | 0 / 1 (0.00%) | 0 / 10 (0.00%)  | 0 / 14 (0.00%) |
| occurrences (all)                | 0             | 0               | 0              |
| Tooth fracture                   |               |                 |                |
| subjects affected / exposed      | 0 / 1 (0.00%) | 0 / 10 (0.00%)  | 0 / 14 (0.00%) |
| occurrences (all)                | 0             | 0               | 0              |
| Urinary tract stoma complication |               |                 |                |
| subjects affected / exposed      | 0 / 1 (0.00%) | 1 / 10 (10.00%) | 0 / 14 (0.00%) |
| occurrences (all)                | 0             | 1               | 0              |
| Cardiac disorders                |               |                 |                |

|                             |               |                 |                |
|-----------------------------|---------------|-----------------|----------------|
| Atrial fibrillation         |               |                 |                |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 10 (0.00%)  | 0 / 14 (0.00%) |
| occurrences (all)           | 0             | 0               | 0              |
| Angina pectoris             |               |                 |                |
| subjects affected / exposed | 0 / 1 (0.00%) | 1 / 10 (10.00%) | 0 / 14 (0.00%) |
| occurrences (all)           | 0             | 1               | 0              |
| Palpitations                |               |                 |                |
| subjects affected / exposed | 0 / 1 (0.00%) | 1 / 10 (10.00%) | 0 / 14 (0.00%) |
| occurrences (all)           | 0             | 1               | 0              |
| Tachycardia                 |               |                 |                |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 10 (0.00%)  | 0 / 14 (0.00%) |
| occurrences (all)           | 0             | 0               | 0              |
| Sinus tachycardia           |               |                 |                |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 10 (0.00%)  | 0 / 14 (0.00%) |
| occurrences (all)           | 0             | 0               | 0              |
| Ventricular arrhythmia      |               |                 |                |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 10 (0.00%)  | 0 / 14 (0.00%) |
| occurrences (all)           | 0             | 0               | 0              |
| Nervous system disorders    |               |                 |                |
| Ageusia                     |               |                 |                |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 10 (0.00%)  | 0 / 14 (0.00%) |
| occurrences (all)           | 0             | 0               | 0              |
| Agnosia                     |               |                 |                |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 10 (0.00%)  | 0 / 14 (0.00%) |
| occurrences (all)           | 0             | 0               | 0              |
| Amnesia                     |               |                 |                |
| subjects affected / exposed | 0 / 1 (0.00%) | 1 / 10 (10.00%) | 0 / 14 (0.00%) |
| occurrences (all)           | 0             | 1               | 0              |
| Cauda equina syndrome       |               |                 |                |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 10 (0.00%)  | 1 / 14 (7.14%) |
| occurrences (all)           | 0             | 0               | 1              |
| Disturbance in attention    |               |                 |                |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 10 (0.00%)  | 0 / 14 (0.00%) |
| occurrences (all)           | 0             | 0               | 0              |
| Dizziness                   |               |                 |                |

|                               |               |                 |                 |
|-------------------------------|---------------|-----------------|-----------------|
| subjects affected / exposed   | 0 / 1 (0.00%) | 0 / 10 (0.00%)  | 0 / 14 (0.00%)  |
| occurrences (all)             | 0             | 0               | 0               |
| Dizziness postural            |               |                 |                 |
| subjects affected / exposed   | 0 / 1 (0.00%) | 0 / 10 (0.00%)  | 1 / 14 (7.14%)  |
| occurrences (all)             | 0             | 0               | 1               |
| Headache                      |               |                 |                 |
| subjects affected / exposed   | 0 / 1 (0.00%) | 0 / 10 (0.00%)  | 1 / 14 (7.14%)  |
| occurrences (all)             | 0             | 0               | 1               |
| Dysgeusia                     |               |                 |                 |
| subjects affected / exposed   | 0 / 1 (0.00%) | 4 / 10 (40.00%) | 3 / 14 (21.43%) |
| occurrences (all)             | 0             | 5               | 3               |
| Motor dysfunction             |               |                 |                 |
| subjects affected / exposed   | 0 / 1 (0.00%) | 0 / 10 (0.00%)  | 0 / 14 (0.00%)  |
| occurrences (all)             | 0             | 0               | 0               |
| Neuropathy peripheral         |               |                 |                 |
| subjects affected / exposed   | 0 / 1 (0.00%) | 0 / 10 (0.00%)  | 0 / 14 (0.00%)  |
| occurrences (all)             | 0             | 0               | 0               |
| Peripheral sensory neuropathy |               |                 |                 |
| subjects affected / exposed   | 0 / 1 (0.00%) | 0 / 10 (0.00%)  | 0 / 14 (0.00%)  |
| occurrences (all)             | 0             | 0               | 0               |
| Paraesthesia                  |               |                 |                 |
| subjects affected / exposed   | 0 / 1 (0.00%) | 0 / 10 (0.00%)  | 0 / 14 (0.00%)  |
| occurrences (all)             | 0             | 0               | 0               |
| Presyncope                    |               |                 |                 |
| subjects affected / exposed   | 0 / 1 (0.00%) | 0 / 10 (0.00%)  | 0 / 14 (0.00%)  |
| occurrences (all)             | 0             | 0               | 0               |
| Radiculopathy                 |               |                 |                 |
| subjects affected / exposed   | 0 / 1 (0.00%) | 0 / 10 (0.00%)  | 0 / 14 (0.00%)  |
| occurrences (all)             | 0             | 0               | 0               |
| Syncope                       |               |                 |                 |
| subjects affected / exposed   | 0 / 1 (0.00%) | 0 / 10 (0.00%)  | 0 / 14 (0.00%)  |
| occurrences (all)             | 0             | 0               | 0               |
| Somnolence                    |               |                 |                 |
| subjects affected / exposed   | 0 / 1 (0.00%) | 0 / 10 (0.00%)  | 0 / 14 (0.00%)  |
| occurrences (all)             | 0             | 0               | 0               |
| Sciatica                      |               |                 |                 |

|                                      |                 |                 |                 |
|--------------------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed          | 0 / 1 (0.00%)   | 0 / 10 (0.00%)  | 0 / 14 (0.00%)  |
| occurrences (all)                    | 0               | 0               | 0               |
| Taste disorder                       |                 |                 |                 |
| subjects affected / exposed          | 0 / 1 (0.00%)   | 0 / 10 (0.00%)  | 0 / 14 (0.00%)  |
| occurrences (all)                    | 0               | 0               | 0               |
| Blood and lymphatic system disorders |                 |                 |                 |
| Anaemia                              |                 |                 |                 |
| subjects affected / exposed          | 1 / 1 (100.00%) | 9 / 10 (90.00%) | 3 / 14 (21.43%) |
| occurrences (all)                    | 4               | 15              | 4               |
| Coagulopathy                         |                 |                 |                 |
| subjects affected / exposed          | 0 / 1 (0.00%)   | 0 / 10 (0.00%)  | 0 / 14 (0.00%)  |
| occurrences (all)                    | 0               | 0               | 0               |
| Eosinophilia                         |                 |                 |                 |
| subjects affected / exposed          | 0 / 1 (0.00%)   | 0 / 10 (0.00%)  | 0 / 14 (0.00%)  |
| occurrences (all)                    | 0               | 0               | 0               |
| Lymph node haemorrhage               |                 |                 |                 |
| subjects affected / exposed          | 0 / 1 (0.00%)   | 0 / 10 (0.00%)  | 0 / 14 (0.00%)  |
| occurrences (all)                    | 0               | 0               | 0               |
| Lymph node pain                      |                 |                 |                 |
| subjects affected / exposed          | 0 / 1 (0.00%)   | 0 / 10 (0.00%)  | 0 / 14 (0.00%)  |
| occurrences (all)                    | 0               | 0               | 0               |
| Lymphadenopathy                      |                 |                 |                 |
| subjects affected / exposed          | 0 / 1 (0.00%)   | 0 / 10 (0.00%)  | 0 / 14 (0.00%)  |
| occurrences (all)                    | 0               | 0               | 0               |
| Neutropenia                          |                 |                 |                 |
| subjects affected / exposed          | 0 / 1 (0.00%)   | 1 / 10 (10.00%) | 0 / 14 (0.00%)  |
| occurrences (all)                    | 0               | 2               | 0               |
| Lymphopenia                          |                 |                 |                 |
| subjects affected / exposed          | 0 / 1 (0.00%)   | 0 / 10 (0.00%)  | 0 / 14 (0.00%)  |
| occurrences (all)                    | 0               | 0               | 0               |
| Thrombocytopenia                     |                 |                 |                 |
| subjects affected / exposed          | 0 / 1 (0.00%)   | 5 / 10 (50.00%) | 5 / 14 (35.71%) |
| occurrences (all)                    | 0               | 11              | 9               |
| Ear and labyrinth disorders          |                 |                 |                 |
| Ear congestion                       |                 |                 |                 |

|  |                      |                     |                      |
|--|----------------------|---------------------|----------------------|
| subjects affected / exposed<br>occurrences (all)   | 0 / 1 (0.00%)<br>0   | 0 / 10 (0.00%)<br>0 | 0 / 14 (0.00%)<br>0  |
| Ear haemorrhage<br>subjects affected / exposed<br>occurrences (all)                                    | 0 / 1 (0.00%)<br>0   | 0 / 10 (0.00%)<br>0 | 0 / 14 (0.00%)<br>0  |
| Ear pain<br>subjects affected / exposed<br>occurrences (all)   | 0 / 1 (0.00%)<br>0   | 0 / 10 (0.00%)<br>0 | 0 / 14 (0.00%)<br>0  |
| Vertigo<br>subjects affected / exposed<br>occurrences (all)  | 0 / 1 (0.00%)<br>0   | 0 / 10 (0.00%)<br>0 | 0 / 14 (0.00%)<br>0  |
| Eye disorders<br>Conjunctival haemorrhage<br>subjects affected / exposed<br>occurrences (all)          | 0 / 1 (0.00%)<br>0   | 0 / 10 (0.00%)<br>0 | 0 / 14 (0.00%)<br>0  |
| Dry eye<br>subjects affected / exposed<br>occurrences (all)  | 0 / 1 (0.00%)<br>0   | 0 / 10 (0.00%)<br>0 | 0 / 14 (0.00%)<br>0  |
| Vitreous haemorrhage<br>subjects affected / exposed<br>occurrences (all)                               | 1 / 1 (100.00%)<br>1 | 0 / 10 (0.00%)<br>0 | 0 / 14 (0.00%)<br>0  |
| Vision blurred<br>subjects affected / exposed<br>occurrences (all)                                     | 0 / 1 (0.00%)<br>0   | 0 / 10 (0.00%)<br>0 | 1 / 14 (7.14%)<br>1  |
| Periorbital oedema<br>subjects affected / exposed<br>occurrences (all)                                 | 0 / 1 (0.00%)<br>0   | 0 / 10 (0.00%)<br>0 | 0 / 14 (0.00%)<br>0  |
| Gastrointestinal disorders<br>Abdominal pain upper<br>subjects affected / exposed<br>occurrences (all) | 0 / 1 (0.00%)<br>0   | 0 / 10 (0.00%)<br>0 | 0 / 14 (0.00%)<br>0  |
| Abdominal pain<br>subjects affected / exposed<br>occurrences (all)                                     | 0 / 1 (0.00%)<br>0   | 0 / 10 (0.00%)<br>0 | 3 / 14 (21.43%)<br>6 |
| Abdominal distension   |                      |                     |                      |

|                             |               |                 |                 |
|-----------------------------|---------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 10 (0.00%)  | 0 / 14 (0.00%)  |
| occurrences (all)           | 0             | 0               | 0               |
| Anal fissure                |               |                 |                 |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 10 (0.00%)  | 0 / 14 (0.00%)  |
| occurrences (all)           | 0             | 0               | 0               |
| Anal haemorrhage            |               |                 |                 |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 10 (0.00%)  | 0 / 14 (0.00%)  |
| occurrences (all)           | 0             | 0               | 0               |
| Aphthous ulcer              |               |                 |                 |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 10 (0.00%)  | 0 / 14 (0.00%)  |
| occurrences (all)           | 0             | 0               | 0               |
| Angular cheilitis           |               |                 |                 |
| subjects affected / exposed | 0 / 1 (0.00%) | 1 / 10 (10.00%) | 0 / 14 (0.00%)  |
| occurrences (all)           | 0             | 1               | 0               |
| Anal inflammation           |               |                 |                 |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 10 (0.00%)  | 0 / 14 (0.00%)  |
| occurrences (all)           | 0             | 0               | 0               |
| Ascites                     |               |                 |                 |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 10 (0.00%)  | 1 / 14 (7.14%)  |
| occurrences (all)           | 0             | 0               | 1               |
| Constipation                |               |                 |                 |
| subjects affected / exposed | 0 / 1 (0.00%) | 3 / 10 (30.00%) | 3 / 14 (21.43%) |
| occurrences (all)           | 0             | 3               | 3               |
| Diarrhoea                   |               |                 |                 |
| subjects affected / exposed | 0 / 1 (0.00%) | 6 / 10 (60.00%) | 8 / 14 (57.14%) |
| occurrences (all)           | 0             | 8               | 16              |
| Dry mouth                   |               |                 |                 |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 10 (0.00%)  | 0 / 14 (0.00%)  |
| occurrences (all)           | 0             | 0               | 0               |
| Dyspepsia                   |               |                 |                 |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 10 (0.00%)  | 0 / 14 (0.00%)  |
| occurrences (all)           | 0             | 0               | 0               |
| Dysphagia                   |               |                 |                 |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 10 (0.00%)  | 0 / 14 (0.00%)  |
| occurrences (all)           | 0             | 0               | 0               |
| Flatulence                  |               |                 |                 |

|                                    |               |                 |                 |
|------------------------------------|---------------|-----------------|-----------------|
| subjects affected / exposed        | 0 / 1 (0.00%) | 0 / 10 (0.00%)  | 0 / 14 (0.00%)  |
| occurrences (all)                  | 0             | 0               | 0               |
| Gastritis                          |               |                 |                 |
| subjects affected / exposed        | 0 / 1 (0.00%) | 0 / 10 (0.00%)  | 0 / 14 (0.00%)  |
| occurrences (all)                  | 0             | 0               | 0               |
| Gastritis erosive                  |               |                 |                 |
| subjects affected / exposed        | 0 / 1 (0.00%) | 0 / 10 (0.00%)  | 0 / 14 (0.00%)  |
| occurrences (all)                  | 0             | 0               | 0               |
| Gastrointestinal disorder          |               |                 |                 |
| subjects affected / exposed        | 0 / 1 (0.00%) | 0 / 10 (0.00%)  | 0 / 14 (0.00%)  |
| occurrences (all)                  | 0             | 0               | 0               |
| Gastrooesophageal reflux disease   |               |                 |                 |
| subjects affected / exposed        | 0 / 1 (0.00%) | 1 / 10 (10.00%) | 0 / 14 (0.00%)  |
| occurrences (all)                  | 0             | 2               | 0               |
| Haemorrhoids                       |               |                 |                 |
| subjects affected / exposed        | 0 / 1 (0.00%) | 0 / 10 (0.00%)  | 0 / 14 (0.00%)  |
| occurrences (all)                  | 0             | 0               | 0               |
| Lip dry                            |               |                 |                 |
| subjects affected / exposed        | 0 / 1 (0.00%) | 0 / 10 (0.00%)  | 0 / 14 (0.00%)  |
| occurrences (all)                  | 0             | 0               | 0               |
| Melaena                            |               |                 |                 |
| subjects affected / exposed        | 0 / 1 (0.00%) | 0 / 10 (0.00%)  | 0 / 14 (0.00%)  |
| occurrences (all)                  | 0             | 0               | 0               |
| Lower gastrointestinal haemorrhage |               |                 |                 |
| subjects affected / exposed        | 0 / 1 (0.00%) | 0 / 10 (0.00%)  | 0 / 14 (0.00%)  |
| occurrences (all)                  | 0             | 0               | 0               |
| Nausea                             |               |                 |                 |
| subjects affected / exposed        | 0 / 1 (0.00%) | 5 / 10 (50.00%) | 6 / 14 (42.86%) |
| occurrences (all)                  | 0             | 5               | 11              |
| Odynophagia                        |               |                 |                 |
| subjects affected / exposed        | 0 / 1 (0.00%) | 0 / 10 (0.00%)  | 0 / 14 (0.00%)  |
| occurrences (all)                  | 0             | 0               | 0               |
| Oral mucosal erythema              |               |                 |                 |
| subjects affected / exposed        | 0 / 1 (0.00%) | 0 / 10 (0.00%)  | 0 / 14 (0.00%)  |
| occurrences (all)                  | 0             | 0               | 0               |
| Retching                           |               |                 |                 |

|  |                 |                 |                 |
|--|-----------------|-----------------|-----------------|
| subjects affected / exposed            | 0 / 1 (0.00%)   | 0 / 10 (0.00%)  | 0 / 14 (0.00%)  |
| occurrences (all)                      | 0               | 0               | 0               |
| Stomatitis                             |                 |                 |                 |
| subjects affected / exposed            | 1 / 1 (100.00%) | 1 / 10 (10.00%) | 0 / 14 (0.00%)  |
| occurrences (all)                      | 1               | 2               | 0               |
| Subileus                               |                 |                 |                 |
| subjects affected / exposed            | 0 / 1 (0.00%)   | 0 / 10 (0.00%)  | 1 / 14 (7.14%)  |
| occurrences (all)                      | 0               | 0               | 1               |
| Toothache                              |                 |                 |                 |
| subjects affected / exposed            | 0 / 1 (0.00%)   | 0 / 10 (0.00%)  | 0 / 14 (0.00%)  |
| occurrences (all)                      | 0               | 0               | 0               |
| Vomiting                               |                 |                 |                 |
| subjects affected / exposed            | 0 / 1 (0.00%)   | 6 / 10 (60.00%) | 3 / 14 (21.43%) |
| occurrences (all)                      | 0               | 6               | 7               |
| Hepatobiliary disorders                |                 |                 |                 |
| Cholangitis                            |                 |                 |                 |
| subjects affected / exposed            | 0 / 1 (0.00%)   | 0 / 10 (0.00%)  | 0 / 14 (0.00%)  |
| occurrences (all)                      | 0               | 0               | 0               |
| Hepatic cytolysis                      |                 |                 |                 |
| subjects affected / exposed            | 0 / 1 (0.00%)   | 0 / 10 (0.00%)  | 0 / 14 (0.00%)  |
| occurrences (all)                      | 0               | 0               | 0               |
| Hepatic pain                           |                 |                 |                 |
| subjects affected / exposed            | 0 / 1 (0.00%)   | 0 / 10 (0.00%)  | 0 / 14 (0.00%)  |
| occurrences (all)                      | 0               | 0               | 0               |
| Skin and subcutaneous tissue disorders |                 |                 |                 |
| Dermatitis psoriasiform                |                 |                 |                 |
| subjects affected / exposed            | 0 / 1 (0.00%)   | 0 / 10 (0.00%)  | 0 / 14 (0.00%)  |
| occurrences (all)                      | 0               | 0               | 0               |
| Dermatitis acneiform                   |                 |                 |                 |
| subjects affected / exposed            | 0 / 1 (0.00%)   | 0 / 10 (0.00%)  | 0 / 14 (0.00%)  |
| occurrences (all)                      | 0               | 0               | 0               |
| Dry skin                               |                 |                 |                 |
| subjects affected / exposed            | 0 / 1 (0.00%)   | 0 / 10 (0.00%)  | 1 / 14 (7.14%)  |
| occurrences (all)                      | 0               | 0               | 1               |
| Intertrigo                             |                 |                 |                 |



|                             |               |                 |                |
|-----------------------------|---------------|-----------------|----------------|
| subjects affected / exposed | 0 / 1 (0.00%) | 1 / 10 (10.00%) | 0 / 14 (0.00%) |
| occurrences (all)           | 0             | 1               | 0              |
| Macule                      |               |                 |                |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 10 (0.00%)  | 0 / 14 (0.00%) |
| occurrences (all)           | 0             | 0               | 0              |
| Night sweats                |               |                 |                |
| subjects affected / exposed | 0 / 1 (0.00%) | 1 / 10 (10.00%) | 0 / 14 (0.00%) |
| occurrences (all)           | 0             | 1               | 0              |
| Eczema                      |               |                 |                |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 10 (0.00%)  | 0 / 14 (0.00%) |
| occurrences (all)           | 0             | 0               | 0              |
| Erythema                    |               |                 |                |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 10 (0.00%)  | 0 / 14 (0.00%) |
| occurrences (all)           | 0             | 0               | 0              |
| Prurigo                     |               |                 |                |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 10 (0.00%)  | 1 / 14 (7.14%) |
| occurrences (all)           | 0             | 0               | 1              |
| Pruritus                    |               |                 |                |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 10 (0.00%)  | 1 / 14 (7.14%) |
| occurrences (all)           | 0             | 0               | 1              |
| Psoriasis                   |               |                 |                |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 10 (0.00%)  | 0 / 14 (0.00%) |
| occurrences (all)           | 0             | 0               | 0              |
| Petechiae                   |               |                 |                |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 10 (0.00%)  | 0 / 14 (0.00%) |
| occurrences (all)           | 0             | 0               | 0              |
| Skin ulcer                  |               |                 |                |
| subjects affected / exposed | 0 / 1 (0.00%) | 1 / 10 (10.00%) | 0 / 14 (0.00%) |
| occurrences (all)           | 0             | 1               | 0              |
| Rash                        |               |                 |                |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 10 (0.00%)  | 0 / 14 (0.00%) |
| occurrences (all)           | 0             | 0               | 0              |
| Rash maculo-papular         |               |                 |                |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 10 (0.00%)  | 0 / 14 (0.00%) |
| occurrences (all)           | 0             | 0               | 0              |
| Purpura                     |               |                 |                |

|   |                      |                      |                      |
|---|----------------------|----------------------|----------------------|
| subjects affected / exposed<br>occurrences (all)  | 1 / 1 (100.00%)<br>1 | 0 / 10 (0.00%)<br>0  | 0 / 14 (0.00%)<br>0  |
| Urticaria<br>subjects affected / exposed<br>occurrences (all)   | 0 / 1 (0.00%)<br>0   | 0 / 10 (0.00%)<br>0  | 0 / 14 (0.00%)<br>0  |
| Renal and urinary disorders<br>Dysuria<br>subjects affected / exposed<br>occurrences (all)                        | 0 / 1 (0.00%)<br>0   | 0 / 10 (0.00%)<br>0  | 0 / 14 (0.00%)<br>0  |
| Haematuria<br>subjects affected / exposed<br>occurrences (all)  | 1 / 1 (100.00%)<br>1 | 3 / 10 (30.00%)<br>4 | 2 / 14 (14.29%)<br>2 |
| Pollakiuria<br>subjects affected / exposed<br>occurrences (all)   | 0 / 1 (0.00%)<br>0   | 2 / 10 (20.00%)<br>2 | 0 / 14 (0.00%)<br>0  |
| Urinary tract pain<br>subjects affected / exposed<br>occurrences (all)  | 0 / 1 (0.00%)<br>0   | 1 / 10 (10.00%)<br>1 | 0 / 14 (0.00%)<br>0  |
| Urinary retention<br>subjects affected / exposed<br>occurrences (all)   | 0 / 1 (0.00%)<br>0   | 1 / 10 (10.00%)<br>1 | 0 / 14 (0.00%)<br>0  |
| Renal failure<br>subjects affected / exposed<br>occurrences (all)   | 0 / 1 (0.00%)<br>0   | 0 / 10 (0.00%)<br>0  | 2 / 14 (14.29%)<br>3 |
| Endocrine disorders<br>Hyperthyroidism<br>subjects affected / exposed<br>occurrences (all)                        | 0 / 1 (0.00%)<br>0   | 0 / 10 (0.00%)<br>0  | 0 / 14 (0.00%)<br>0  |
| Musculoskeletal and connective tissue disorders<br>Arthralgia<br>subjects affected / exposed<br>occurrences (all) | 0 / 1 (0.00%)<br>0   | 1 / 10 (10.00%)<br>2 | 0 / 14 (0.00%)<br>0  |
| Back pain<br>subjects affected / exposed<br>occurrences (all)   | 0 / 1 (0.00%)<br>0   | 1 / 10 (10.00%)<br>1 | 1 / 14 (7.14%)<br>1  |
| Bone pain   |                      |                      |                      |

|                             |               |                 |                 |
|-----------------------------|---------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 1 (0.00%) | 1 / 10 (10.00%) | 0 / 14 (0.00%)  |
| occurrences (all)           | 0             | 1               | 0               |
| Flank pain                  |               |                 |                 |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 10 (0.00%)  | 0 / 14 (0.00%)  |
| occurrences (all)           | 0             | 0               | 0               |
| Groin pain                  |               |                 |                 |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 10 (0.00%)  | 0 / 14 (0.00%)  |
| occurrences (all)           | 0             | 0               | 0               |
| Muscular weakness           |               |                 |                 |
| subjects affected / exposed | 0 / 1 (0.00%) | 1 / 10 (10.00%) | 0 / 14 (0.00%)  |
| occurrences (all)           | 0             | 2               | 0               |
| Muscle spasms               |               |                 |                 |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 10 (0.00%)  | 2 / 14 (14.29%) |
| occurrences (all)           | 0             | 0               | 2               |
| Myalgia                     |               |                 |                 |
| subjects affected / exposed | 0 / 1 (0.00%) | 1 / 10 (10.00%) | 0 / 14 (0.00%)  |
| occurrences (all)           | 0             | 1               | 0               |
| Neck pain                   |               |                 |                 |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 10 (0.00%)  | 0 / 14 (0.00%)  |
| occurrences (all)           | 0             | 0               | 0               |
| Pain in extremity           |               |                 |                 |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 10 (0.00%)  | 0 / 14 (0.00%)  |
| occurrences (all)           | 0             | 0               | 0               |
| Pubic pain                  |               |                 |                 |
| subjects affected / exposed | 0 / 1 (0.00%) | 1 / 10 (10.00%) | 0 / 14 (0.00%)  |
| occurrences (all)           | 0             | 1               | 0               |
| Infections and infestations |               |                 |                 |
| Bronchitis                  |               |                 |                 |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 10 (0.00%)  | 0 / 14 (0.00%)  |
| occurrences (all)           | 0             | 0               | 0               |
| Bronchitis viral            |               |                 |                 |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 10 (0.00%)  | 1 / 14 (7.14%)  |
| occurrences (all)           | 0             | 0               | 1               |
| Clostridial infection       |               |                 |                 |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 10 (0.00%)  | 0 / 14 (0.00%)  |
| occurrences (all)           | 0             | 0               | 0               |

|                                     |               |                |                |
|-------------------------------------|---------------|----------------|----------------|
| Clostridium difficile colitis       |               |                |                |
| subjects affected / exposed         | 0 / 1 (0.00%) | 0 / 10 (0.00%) | 0 / 14 (0.00%) |
| occurrences (all)                   | 0             | 0              | 0              |
| Conjunctivitis                      |               |                |                |
| subjects affected / exposed         | 0 / 1 (0.00%) | 0 / 10 (0.00%) | 0 / 14 (0.00%) |
| occurrences (all)                   | 0             | 0              | 0              |
| Erysipelas                          |               |                |                |
| subjects affected / exposed         | 0 / 1 (0.00%) | 0 / 10 (0.00%) | 0 / 14 (0.00%) |
| occurrences (all)                   | 0             | 0              | 0              |
| Diverticulitis                      |               |                |                |
| subjects affected / exposed         | 0 / 1 (0.00%) | 0 / 10 (0.00%) | 0 / 14 (0.00%) |
| occurrences (all)                   | 0             | 0              | 0              |
| Cystitis                            |               |                |                |
| subjects affected / exposed         | 0 / 1 (0.00%) | 0 / 10 (0.00%) | 0 / 14 (0.00%) |
| occurrences (all)                   | 0             | 0              | 0              |
| Gastroenteritis                     |               |                |                |
| subjects affected / exposed         | 0 / 1 (0.00%) | 0 / 10 (0.00%) | 0 / 14 (0.00%) |
| occurrences (all)                   | 0             | 0              | 0              |
| Folliculitis                        |               |                |                |
| subjects affected / exposed         | 0 / 1 (0.00%) | 0 / 10 (0.00%) | 0 / 14 (0.00%) |
| occurrences (all)                   | 0             | 0              | 0              |
| Escherichia urinary tract infection |               |                |                |
| subjects affected / exposed         | 0 / 1 (0.00%) | 0 / 10 (0.00%) | 0 / 14 (0.00%) |
| occurrences (all)                   | 0             | 0              | 0              |
| Genital herpes simplex              |               |                |                |
| subjects affected / exposed         | 0 / 1 (0.00%) | 0 / 10 (0.00%) | 0 / 14 (0.00%) |
| occurrences (all)                   | 0             | 0              | 0              |
| Genital infection fungal            |               |                |                |
| subjects affected / exposed         | 0 / 1 (0.00%) | 0 / 10 (0.00%) | 0 / 14 (0.00%) |
| occurrences (all)                   | 0             | 0              | 0              |
| Herpes dermatitis                   |               |                |                |
| subjects affected / exposed         | 0 / 1 (0.00%) | 0 / 10 (0.00%) | 0 / 14 (0.00%) |
| occurrences (all)                   | 0             | 0              | 0              |
| Impetigo                            |               |                |                |
| subjects affected / exposed         | 0 / 1 (0.00%) | 0 / 10 (0.00%) | 1 / 14 (7.14%) |
| occurrences (all)                   | 0             | 0              | 1              |

|                                       |               |                 |                |
|---------------------------------------|---------------|-----------------|----------------|
| Herpes zoster                         |               |                 |                |
| subjects affected / exposed           | 0 / 1 (0.00%) | 1 / 10 (10.00%) | 0 / 14 (0.00%) |
| occurrences (all)                     | 0             | 1               | 0              |
| Influenza                             |               |                 |                |
| subjects affected / exposed           | 0 / 1 (0.00%) | 0 / 10 (0.00%)  | 0 / 14 (0.00%) |
| occurrences (all)                     | 0             | 0               | 0              |
| Infection                             |               |                 |                |
| subjects affected / exposed           | 0 / 1 (0.00%) | 0 / 10 (0.00%)  | 0 / 14 (0.00%) |
| occurrences (all)                     | 0             | 0               | 0              |
| Nasopharyngitis                       |               |                 |                |
| subjects affected / exposed           | 0 / 1 (0.00%) | 0 / 10 (0.00%)  | 0 / 14 (0.00%) |
| occurrences (all)                     | 0             | 0               | 0              |
| Oesophageal infection                 |               |                 |                |
| subjects affected / exposed           | 0 / 1 (0.00%) | 0 / 10 (0.00%)  | 0 / 14 (0.00%) |
| occurrences (all)                     | 0             | 0               | 0              |
| Pharyngitis                           |               |                 |                |
| subjects affected / exposed           | 0 / 1 (0.00%) | 0 / 10 (0.00%)  | 0 / 14 (0.00%) |
| occurrences (all)                     | 0             | 0               | 0              |
| Oral herpes                           |               |                 |                |
| subjects affected / exposed           | 0 / 1 (0.00%) | 0 / 10 (0.00%)  | 0 / 14 (0.00%) |
| occurrences (all)                     | 0             | 0               | 0              |
| Pneumonia                             |               |                 |                |
| subjects affected / exposed           | 0 / 1 (0.00%) | 0 / 10 (0.00%)  | 0 / 14 (0.00%) |
| occurrences (all)                     | 0             | 0               | 0              |
| Rash pustular                         |               |                 |                |
| subjects affected / exposed           | 0 / 1 (0.00%) | 0 / 10 (0.00%)  | 0 / 14 (0.00%) |
| occurrences (all)                     | 0             | 0               | 0              |
| Respiratory tract infection           |               |                 |                |
| subjects affected / exposed           | 0 / 1 (0.00%) | 0 / 10 (0.00%)  | 0 / 14 (0.00%) |
| occurrences (all)                     | 0             | 0               | 0              |
| Respiratory tract infection bacterial |               |                 |                |
| subjects affected / exposed           | 0 / 1 (0.00%) | 0 / 10 (0.00%)  | 0 / 14 (0.00%) |
| occurrences (all)                     | 0             | 0               | 0              |
| Sinusitis                             |               |                 |                |
| subjects affected / exposed           | 0 / 1 (0.00%) | 0 / 10 (0.00%)  | 0 / 14 (0.00%) |
| occurrences (all)                     | 0             | 0               | 0              |

|  |                      |                      |                      |
|--|----------------------|----------------------|----------------------|
| Tooth abscess<br>subjects affected / exposed<br>occurrences (all)                                  | 0 / 1 (0.00%)<br>0   | 0 / 10 (0.00%)<br>0  | 0 / 14 (0.00%)<br>0  |
| Tooth infection<br>subjects affected / exposed<br>occurrences (all)                                | 0 / 1 (0.00%)<br>0   | 0 / 10 (0.00%)<br>0  | 0 / 14 (0.00%)<br>0  |
| Tracheitis<br>subjects affected / exposed<br>occurrences (all)                                     | 0 / 1 (0.00%)<br>0   | 0 / 10 (0.00%)<br>0  | 0 / 14 (0.00%)<br>0  |
| Upper respiratory tract infection<br>subjects affected / exposed<br>occurrences (all)              | 0 / 1 (0.00%)<br>0   | 0 / 10 (0.00%)<br>0  | 0 / 14 (0.00%)<br>0  |
| Urinary tract infection enterococcal<br>subjects affected / exposed<br>occurrences (all)           | 0 / 1 (0.00%)<br>0   | 0 / 10 (0.00%)<br>0  | 0 / 14 (0.00%)<br>0  |
| Urinary tract infection<br>subjects affected / exposed<br>occurrences (all)                        | 0 / 1 (0.00%)<br>0   | 0 / 10 (0.00%)<br>0  | 1 / 14 (7.14%)<br>1  |
| Mucosal infection<br>subjects affected / exposed<br>occurrences (all)                              | 0 / 1 (0.00%)<br>0   | 0 / 10 (0.00%)<br>0  | 0 / 14 (0.00%)<br>0  |
| Stoma site infection<br>subjects affected / exposed<br>occurrences (all)                           | 0 / 1 (0.00%)<br>0   | 0 / 10 (0.00%)<br>0  | 0 / 14 (0.00%)<br>0  |
| Metabolism and nutrition disorders<br>Acidosis<br>subjects affected / exposed<br>occurrences (all) | 0 / 1 (0.00%)<br>0   | 0 / 10 (0.00%)<br>0  | 0 / 14 (0.00%)<br>0  |
| Decreased appetite<br>subjects affected / exposed<br>occurrences (all)                             | 1 / 1 (100.00%)<br>1 | 6 / 10 (60.00%)<br>8 | 7 / 14 (50.00%)<br>8 |
| Cell death<br>subjects affected / exposed<br>occurrences (all)                                     | 0 / 1 (0.00%)<br>0   | 0 / 10 (0.00%)<br>0  | 0 / 14 (0.00%)<br>0  |
| Dehydration  |                      |                      |                      |

|                             |               |                 |                 |
|-----------------------------|---------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 10 (0.00%)  | 0 / 14 (0.00%)  |
| occurrences (all)           | 0             | 0               | 0               |
| Fluid retention             |               |                 |                 |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 10 (0.00%)  | 0 / 14 (0.00%)  |
| occurrences (all)           | 0             | 0               | 0               |
| Folate deficiency           |               |                 |                 |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 10 (0.00%)  | 0 / 14 (0.00%)  |
| occurrences (all)           | 0             | 0               | 0               |
| Gout                        |               |                 |                 |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 10 (0.00%)  | 0 / 14 (0.00%)  |
| occurrences (all)           | 0             | 0               | 0               |
| Hypercalcaemia              |               |                 |                 |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 10 (0.00%)  | 0 / 14 (0.00%)  |
| occurrences (all)           | 0             | 0               | 0               |
| Hyperkalaemia               |               |                 |                 |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 10 (0.00%)  | 1 / 14 (7.14%)  |
| occurrences (all)           | 0             | 0               | 1               |
| Hyperglycaemia              |               |                 |                 |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 10 (0.00%)  | 1 / 14 (7.14%)  |
| occurrences (all)           | 0             | 0               | 1               |
| Hyperphosphataemia          |               |                 |                 |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 10 (0.00%)  | 0 / 14 (0.00%)  |
| occurrences (all)           | 0             | 0               | 0               |
| Hypoalbuminaemia            |               |                 |                 |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 10 (0.00%)  | 0 / 14 (0.00%)  |
| occurrences (all)           | 0             | 0               | 0               |
| Hypocalcaemia               |               |                 |                 |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 10 (0.00%)  | 1 / 14 (7.14%)  |
| occurrences (all)           | 0             | 0               | 1               |
| Hypokalaemia                |               |                 |                 |
| subjects affected / exposed | 0 / 1 (0.00%) | 1 / 10 (10.00%) | 2 / 14 (14.29%) |
| occurrences (all)           | 0             | 1               | 2               |
| Hypomagnesaemia             |               |                 |                 |
| subjects affected / exposed | 0 / 1 (0.00%) | 1 / 10 (10.00%) | 0 / 14 (0.00%)  |
| occurrences (all)           | 0             | 1               | 0               |
| Hyponatraemia               |               |                 |                 |

|                             |               |                 |                |
|-----------------------------|---------------|-----------------|----------------|
| subjects affected / exposed | 0 / 1 (0.00%) | 1 / 10 (10.00%) | 1 / 14 (7.14%) |
| occurrences (all)           | 0             | 1               | 1              |
| Hypophosphataemia           |               |                 |                |
| subjects affected / exposed | 0 / 1 (0.00%) | 2 / 10 (20.00%) | 0 / 14 (0.00%) |
| occurrences (all)           | 0             | 2               | 0              |
| Malnutrition                |               |                 |                |
| subjects affected / exposed | 0 / 1 (0.00%) | 0 / 10 (0.00%)  | 0 / 14 (0.00%) |
| occurrences (all)           | 0             | 0               | 0              |

|   |   |  |  |
|---|---|--|--|
| <b>Non-serious adverse events</b>                                   | Phase Ib - Schedule C: BI 894999 7/3.5 mg (NC patients) |  |  |
| Total subjects affected by non-serious adverse events               |   |  |  |
| subjects affected / exposed   | 1 / 1 (100.00%)   |  |  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |   |  |  |
| Tumour pain   |   |  |  |
| subjects affected / exposed   | 0 / 1 (0.00%)   |  |  |
| occurrences (all)   | 0   |  |  |
| Vascular disorders  |   |  |  |
| Hypotension   |   |  |  |
| subjects affected / exposed   | 0 / 1 (0.00%)   |  |  |
| occurrences (all)   | 0   |  |  |
| Hypertension  |   |  |  |
| subjects affected / exposed   | 0 / 1 (0.00%)   |  |  |
| occurrences (all)   | 0   |  |  |
| Haematoma   |   |  |  |
| subjects affected / exposed   | 0 / 1 (0.00%)   |  |  |
| occurrences (all)   | 0   |  |  |
| Orthostatic hypotension   |   |  |  |
| subjects affected / exposed   | 0 / 1 (0.00%)   |  |  |
| occurrences (all)   | 0   |  |  |
| Pallor  |   |  |  |
| subjects affected / exposed   | 0 / 1 (0.00%)   |  |  |
| occurrences (all)   | 0   |  |  |
| General disorders and administration site conditions                |   |  |  |
| Chest discomfort  |   |  |  |



|                                       |               |  |  |
|---------------------------------------|---------------|--|--|
| subjects affected / exposed           | 0 / 1 (0.00%) |  |  |
| occurrences (all)                     | 0             |  |  |
| Asthenia                              |               |  |  |
| subjects affected / exposed           | 0 / 1 (0.00%) |  |  |
| occurrences (all)                     | 0             |  |  |
| Chest pain                            |               |  |  |
| subjects affected / exposed           | 0 / 1 (0.00%) |  |  |
| occurrences (all)                     | 0             |  |  |
| Fatigue                               |               |  |  |
| subjects affected / exposed           | 0 / 1 (0.00%) |  |  |
| occurrences (all)                     | 0             |  |  |
| Facial pain                           |               |  |  |
| subjects affected / exposed           | 0 / 1 (0.00%) |  |  |
| occurrences (all)                     | 0             |  |  |
| Chills                                |               |  |  |
| subjects affected / exposed           | 0 / 1 (0.00%) |  |  |
| occurrences (all)                     | 0             |  |  |
| Gait disturbance                      |               |  |  |
| subjects affected / exposed           | 0 / 1 (0.00%) |  |  |
| occurrences (all)                     | 0             |  |  |
| General physical health deterioration |               |  |  |
| subjects affected / exposed           | 0 / 1 (0.00%) |  |  |
| occurrences (all)                     | 0             |  |  |
| Generalised oedema                    |               |  |  |
| subjects affected / exposed           | 0 / 1 (0.00%) |  |  |
| occurrences (all)                     | 0             |  |  |
| Malaise                               |               |  |  |
| subjects affected / exposed           | 0 / 1 (0.00%) |  |  |
| occurrences (all)                     | 0             |  |  |
| Hypothermia                           |               |  |  |
| subjects affected / exposed           | 0 / 1 (0.00%) |  |  |
| occurrences (all)                     | 0             |  |  |
| Oedema peripheral                     |               |  |  |
| subjects affected / exposed           | 0 / 1 (0.00%) |  |  |
| occurrences (all)                     | 0             |  |  |
| Non-cardiac chest pain                |               |  |  |

|  |               |  |  |
|--|---------------|--|--|
| subjects affected / exposed              | 0 / 1 (0.00%) |  |  |
| occurrences (all)                        | 0             |  |  |
| Pain                                     |               |  |  |
| subjects affected / exposed              | 0 / 1 (0.00%) |  |  |
| occurrences (all)                        | 0             |  |  |
| Pyrexia                                  |               |  |  |
| subjects affected / exposed              | 0 / 1 (0.00%) |  |  |
| occurrences (all)                        | 0             |  |  |
| Peripheral swelling                      |               |  |  |
| subjects affected / exposed              | 0 / 1 (0.00%) |  |  |
| occurrences (all)                        | 0             |  |  |
| Immune system disorders                  |               |  |  |
| Hypersensitivity                         |               |  |  |
| subjects affected / exposed              | 0 / 1 (0.00%) |  |  |
| occurrences (all)                        | 0             |  |  |
| Iodine allergy                           |               |  |  |
| subjects affected / exposed              | 0 / 1 (0.00%) |  |  |
| occurrences (all)                        | 0             |  |  |
| Reproductive system and breast disorders |               |  |  |
| Erectile dysfunction                     |               |  |  |
| subjects affected / exposed              | 0 / 1 (0.00%) |  |  |
| occurrences (all)                        | 0             |  |  |
| Heavy menstrual bleeding                 |               |  |  |
| subjects affected / exposed              | 0 / 1 (0.00%) |  |  |
| occurrences (all)                        | 0             |  |  |
| Oedema genital                           |               |  |  |
| subjects affected / exposed              | 0 / 1 (0.00%) |  |  |
| occurrences (all)                        | 0             |  |  |
| Perineal pain                            |               |  |  |
| subjects affected / exposed              | 0 / 1 (0.00%) |  |  |
| occurrences (all)                        | 0             |  |  |
| Scrotal oedema                           |               |  |  |
| subjects affected / exposed              | 0 / 1 (0.00%) |  |  |
| occurrences (all)                        | 0             |  |  |
| Testicular pain                          |               |  |  |

|   |               |  |  |
|---|---------------|--|--|
| subjects affected / exposed                     | 0 / 1 (0.00%) |  |  |
| occurrences (all)                               | 0             |  |  |
| Vulvovaginal discomfort                         |               |  |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) |  |  |
| occurrences (all)                               | 0             |  |  |
| Vaginal haemorrhage                             |               |  |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) |  |  |
| occurrences (all)                               | 0             |  |  |
| Respiratory, thoracic and mediastinal disorders |               |  |  |
| Atelectasis                                     |               |  |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) |  |  |
| occurrences (all)                               | 0             |  |  |
| Dysphonia                                       |               |  |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) |  |  |
| occurrences (all)                               | 0             |  |  |
| Cough   |               |  |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) |  |  |
| occurrences (all)                               | 0             |  |  |
| Dyspnoea  |               |  |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) |  |  |
| occurrences (all)                               | 0             |  |  |
| Dyspnoea exertional                             |               |  |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) |  |  |
| occurrences (all)                               | 0             |  |  |
| Epistaxis                                       |               |  |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) |  |  |
| occurrences (all)                               | 0             |  |  |
| Laryngeal inflammation                          |               |  |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) |  |  |
| occurrences (all)                               | 0             |  |  |
| Haemoptysis                                     |               |  |  |
| subjects affected / exposed                     | 0 / 1 (0.00%) |  |  |
| occurrences (all)                               | 0             |  |  |
| Nasal discomfort                                |               |  |  |

|                              |                 |  |  |
|------------------------------|-----------------|--|--|
| subjects affected / exposed  | 0 / 1 (0.00%)   |  |  |
| occurrences (all)            | 0               |  |  |
| Oropharyngeal pain           |                 |  |  |
| subjects affected / exposed  | 0 / 1 (0.00%)   |  |  |
| occurrences (all)            | 0               |  |  |
| Pharyngeal inflammation      |                 |  |  |
| subjects affected / exposed  | 0 / 1 (0.00%)   |  |  |
| occurrences (all)            | 0               |  |  |
| Pleural effusion             |                 |  |  |
| subjects affected / exposed  | 0 / 1 (0.00%)   |  |  |
| occurrences (all)            | 0               |  |  |
| Pleuritic pain               |                 |  |  |
| subjects affected / exposed  | 0 / 1 (0.00%)   |  |  |
| occurrences (all)            | 0               |  |  |
| Productive cough             |                 |  |  |
| subjects affected / exposed  | 1 / 1 (100.00%) |  |  |
| occurrences (all)            | 1               |  |  |
| Rhinorrhoea                  |                 |  |  |
| subjects affected / exposed  | 0 / 1 (0.00%)   |  |  |
| occurrences (all)            | 0               |  |  |
| Respiratory tract congestion |                 |  |  |
| subjects affected / exposed  | 0 / 1 (0.00%)   |  |  |
| occurrences (all)            | 0               |  |  |
| Wheezing                     |                 |  |  |
| subjects affected / exposed  | 0 / 1 (0.00%)   |  |  |
| occurrences (all)            | 0               |  |  |
| Psychiatric disorders        |                 |  |  |
| Affective disorder           |                 |  |  |
| subjects affected / exposed  | 0 / 1 (0.00%)   |  |  |
| occurrences (all)            | 0               |  |  |
| Agitation                    |                 |  |  |
| subjects affected / exposed  | 0 / 1 (0.00%)   |  |  |
| occurrences (all)            | 0               |  |  |
| Anxiety                      |                 |  |  |
| subjects affected / exposed  | 0 / 1 (0.00%)   |  |  |
| occurrences (all)            | 0               |  |  |

|   |                 |  |  |
|---|-----------------|--|--|
| Confusional state                               |                 |  |  |
| subjects affected / exposed                     | 0 / 1 (0.00%)   |  |  |
| occurrences (all)                               | 0               |  |  |
| Depression                                      |                 |  |  |
| subjects affected / exposed                     | 0 / 1 (0.00%)   |  |  |
| occurrences (all)                               | 0               |  |  |
| Insomnia  |                 |  |  |
| subjects affected / exposed                     | 0 / 1 (0.00%)   |  |  |
| occurrences (all)                               | 0               |  |  |
| Hallucination                                   |                 |  |  |
| subjects affected / exposed                     | 0 / 1 (0.00%)   |  |  |
| occurrences (all)                               | 0               |  |  |
| Personality change                              |                 |  |  |
| subjects affected / exposed                     | 0 / 1 (0.00%)   |  |  |
| occurrences (all)                               | 0               |  |  |
| Sleep disorder                                  |                 |  |  |
| subjects affected / exposed                     | 0 / 1 (0.00%)   |  |  |
| occurrences (all)                               | 0               |  |  |
| Investigations                                  |                 |  |  |
| Activated partial thromboplastin time prolonged |                 |  |  |
| subjects affected / exposed                     | 1 / 1 (100.00%) |  |  |
| occurrences (all)                               | 1               |  |  |
| Activated partial thromboplastin time shortened |                 |  |  |
| subjects affected / exposed                     | 0 / 1 (0.00%)   |  |  |
| occurrences (all)                               | 0               |  |  |
| Alanine aminotransferase increased              |                 |  |  |
| subjects affected / exposed                     | 0 / 1 (0.00%)   |  |  |
| occurrences (all)                               | 0               |  |  |
| Aspartate aminotransferase increased            |                 |  |  |
| subjects affected / exposed                     | 1 / 1 (100.00%) |  |  |
| occurrences (all)                               | 2               |  |  |
| Blood alkaline phosphatase increased            |                 |  |  |
| subjects affected / exposed                     | 0 / 1 (0.00%)   |  |  |
| occurrences (all)                               | 0               |  |  |
| Blood antidiuretic hormone                      |                 |  |  |

|  |                 |  |  |
|--|-----------------|--|--|
| decreased                              |                 |  |  |
| subjects affected / exposed            | 0 / 1 (0.00%)   |  |  |
| occurrences (all)                      | 0               |  |  |
| Blood bilirubin increased              |                 |  |  |
| subjects affected / exposed            | 1 / 1 (100.00%) |  |  |
| occurrences (all)                      | 2               |  |  |
| Blood creatine phosphokinase increased |                 |  |  |
| subjects affected / exposed            | 0 / 1 (0.00%)   |  |  |
| occurrences (all)                      | 0               |  |  |
| Blood creatinine increased             |                 |  |  |
| subjects affected / exposed            | 0 / 1 (0.00%)   |  |  |
| occurrences (all)                      | 0               |  |  |
| Blood magnesium decreased              |                 |  |  |
| subjects affected / exposed            | 0 / 1 (0.00%)   |  |  |
| occurrences (all)                      | 0               |  |  |
| Blood glucose increased                |                 |  |  |
| subjects affected / exposed            | 0 / 1 (0.00%)   |  |  |
| occurrences (all)                      | 0               |  |  |
| C-reactive protein increased           |                 |  |  |
| subjects affected / exposed            | 0 / 1 (0.00%)   |  |  |
| occurrences (all)                      | 0               |  |  |
| Cardiac murmur                         |                 |  |  |
| subjects affected / exposed            | 0 / 1 (0.00%)   |  |  |
| occurrences (all)                      | 0               |  |  |
| Cortisol increased                     |                 |  |  |
| subjects affected / exposed            | 0 / 1 (0.00%)   |  |  |
| occurrences (all)                      | 0               |  |  |
| Echocardiogram abnormal                |                 |  |  |
| subjects affected / exposed            | 0 / 1 (0.00%)   |  |  |
| occurrences (all)                      | 0               |  |  |
| Electrocardiogram PR prolongation      |                 |  |  |
| subjects affected / exposed            | 0 / 1 (0.00%)   |  |  |
| occurrences (all)                      | 0               |  |  |
| Ejection fraction decreased            |                 |  |  |

|  |                 |  |  |
|--|-----------------|--|--|
| subjects affected / exposed              | 0 / 1 (0.00%)   |  |  |
| occurrences (all)                        | 0               |  |  |
| Electrocardiogram ST segment elevation   |                 |  |  |
| subjects affected / exposed              | 0 / 1 (0.00%)   |  |  |
| occurrences (all)                        | 0               |  |  |
| Gamma-glutamyltransferase increased      |                 |  |  |
| subjects affected / exposed              | 0 / 1 (0.00%)   |  |  |
| occurrences (all)                        | 0               |  |  |
| Electrocardiogram T wave inversion       |                 |  |  |
| subjects affected / exposed              | 0 / 1 (0.00%)   |  |  |
| occurrences (all)                        | 0               |  |  |
| International normalised ratio increased |                 |  |  |
| subjects affected / exposed              | 1 / 1 (100.00%) |  |  |
| occurrences (all)                        | 1               |  |  |
| Lymphocyte count decreased               |                 |  |  |
| subjects affected / exposed              | 0 / 1 (0.00%)   |  |  |
| occurrences (all)                        | 0               |  |  |
| Neutrophil count decreased               |                 |  |  |
| subjects affected / exposed              | 0 / 1 (0.00%)   |  |  |
| occurrences (all)                        | 0               |  |  |
| Platelet count decreased                 |                 |  |  |
| subjects affected / exposed              | 0 / 1 (0.00%)   |  |  |
| occurrences (all)                        | 0               |  |  |
| Prothrombin level decreased              |                 |  |  |
| subjects affected / exposed              | 0 / 1 (0.00%)   |  |  |
| occurrences (all)                        | 0               |  |  |
| Troponin I increased                     |                 |  |  |
| subjects affected / exposed              | 0 / 1 (0.00%)   |  |  |
| occurrences (all)                        | 0               |  |  |
| Troponin T increased                     |                 |  |  |
| subjects affected / exposed              | 0 / 1 (0.00%)   |  |  |
| occurrences (all)                        | 0               |  |  |
| Troponin increased                       |                 |  |  |

|  |               |  |  |
|--|---------------|--|--|
| subjects affected / exposed                    | 0 / 1 (0.00%) |  |  |
| occurrences (all)                              | 0             |  |  |
| Urine output decreased                         |               |  |  |
| subjects affected / exposed                    | 0 / 1 (0.00%) |  |  |
| occurrences (all)                              | 0             |  |  |
| Weight decreased                               |               |  |  |
| subjects affected / exposed                    | 0 / 1 (0.00%) |  |  |
| occurrences (all)                              | 0             |  |  |
| White blood cell count decreased               |               |  |  |
| subjects affected / exposed                    | 0 / 1 (0.00%) |  |  |
| occurrences (all)                              | 0             |  |  |
| Injury, poisoning and procedural complications |               |  |  |
| Contusion                                      |               |  |  |
| subjects affected / exposed                    | 0 / 1 (0.00%) |  |  |
| occurrences (all)                              | 0             |  |  |
| Face injury                                    |               |  |  |
| subjects affected / exposed                    | 0 / 1 (0.00%) |  |  |
| occurrences (all)                              | 0             |  |  |
| Infusion related reaction                      |               |  |  |
| subjects affected / exposed                    | 0 / 1 (0.00%) |  |  |
| occurrences (all)                              | 0             |  |  |
| Limb injury                                    |               |  |  |
| subjects affected / exposed                    | 0 / 1 (0.00%) |  |  |
| occurrences (all)                              | 0             |  |  |
| Muscle rupture                                 |               |  |  |
| subjects affected / exposed                    | 0 / 1 (0.00%) |  |  |
| occurrences (all)                              | 0             |  |  |
| Overdose                                       |               |  |  |
| subjects affected / exposed                    | 0 / 1 (0.00%) |  |  |
| occurrences (all)                              | 0             |  |  |
| Post procedural haematoma                      |               |  |  |
| subjects affected / exposed                    | 0 / 1 (0.00%) |  |  |
| occurrences (all)                              | 0             |  |  |
| Skin abrasion                                  |               |  |  |



|                                  |                 |  |  |
|----------------------------------|-----------------|--|--|
| subjects affected / exposed      | 0 / 1 (0.00%)   |  |  |
| occurrences (all)                | 0               |  |  |
| Procedural pain                  |                 |  |  |
| subjects affected / exposed      | 0 / 1 (0.00%)   |  |  |
| occurrences (all)                | 0               |  |  |
| Subcutaneous haematoma           |                 |  |  |
| subjects affected / exposed      | 0 / 1 (0.00%)   |  |  |
| occurrences (all)                | 0               |  |  |
| Skin laceration                  |                 |  |  |
| subjects affected / exposed      | 0 / 1 (0.00%)   |  |  |
| occurrences (all)                | 0               |  |  |
| Tongue injury                    |                 |  |  |
| subjects affected / exposed      | 0 / 1 (0.00%)   |  |  |
| occurrences (all)                | 0               |  |  |
| Tooth fracture                   |                 |  |  |
| subjects affected / exposed      | 0 / 1 (0.00%)   |  |  |
| occurrences (all)                | 0               |  |  |
| Urinary tract stoma complication |                 |  |  |
| subjects affected / exposed      | 0 / 1 (0.00%)   |  |  |
| occurrences (all)                | 0               |  |  |
| Cardiac disorders                |                 |  |  |
| Atrial fibrillation              |                 |  |  |
| subjects affected / exposed      | 1 / 1 (100.00%) |  |  |
| occurrences (all)                | 1               |  |  |
| Angina pectoris                  |                 |  |  |
| subjects affected / exposed      | 0 / 1 (0.00%)   |  |  |
| occurrences (all)                | 0               |  |  |
| Palpitations                     |                 |  |  |
| subjects affected / exposed      | 0 / 1 (0.00%)   |  |  |
| occurrences (all)                | 0               |  |  |
| Tachycardia                      |                 |  |  |
| subjects affected / exposed      | 0 / 1 (0.00%)   |  |  |
| occurrences (all)                | 0               |  |  |
| Sinus tachycardia                |                 |  |  |
| subjects affected / exposed      | 0 / 1 (0.00%)   |  |  |
| occurrences (all)                | 0               |  |  |

|  |                    |  |  |
|--|--------------------|--|--|
| Ventricular arrhythmia<br>subjects affected / exposed<br>occurrences (all)   | 0 / 1 (0.00%)<br>0 |  |  |
| Nervous system disorders   |                    |  |  |
| Ageusia<br>subjects affected / exposed<br>occurrences (all)                  | 0 / 1 (0.00%)<br>0 |  |  |
| Agnosia<br>subjects affected / exposed<br>occurrences (all)                  | 0 / 1 (0.00%)<br>0 |  |  |
| Amnesia<br>subjects affected / exposed<br>occurrences (all)                  | 0 / 1 (0.00%)<br>0 |  |  |
| Cauda equina syndrome<br>subjects affected / exposed<br>occurrences (all)    | 0 / 1 (0.00%)<br>0 |  |  |
| Disturbance in attention<br>subjects affected / exposed<br>occurrences (all) | 0 / 1 (0.00%)<br>0 |  |  |
| Dizziness<br>subjects affected / exposed<br>occurrences (all)                | 0 / 1 (0.00%)<br>0 |  |  |
| Dizziness postural<br>subjects affected / exposed<br>occurrences (all)       | 0 / 1 (0.00%)<br>0 |  |  |
| Headache<br>subjects affected / exposed<br>occurrences (all)                 | 0 / 1 (0.00%)<br>0 |  |  |
| Dysgeusia<br>subjects affected / exposed<br>occurrences (all)                | 0 / 1 (0.00%)<br>0 |  |  |
| Motor dysfunction<br>subjects affected / exposed<br>occurrences (all)        | 0 / 1 (0.00%)<br>0 |  |  |
| Neuropathy peripheral  |                    |  |  |

|                                      |               |  |  |
|--------------------------------------|---------------|--|--|
| subjects affected / exposed          | 0 / 1 (0.00%) |  |  |
| occurrences (all)                    | 0             |  |  |
| Peripheral sensory neuropathy        |               |  |  |
| subjects affected / exposed          | 0 / 1 (0.00%) |  |  |
| occurrences (all)                    | 0             |  |  |
| Paraesthesia                         |               |  |  |
| subjects affected / exposed          | 0 / 1 (0.00%) |  |  |
| occurrences (all)                    | 0             |  |  |
| Presyncope                           |               |  |  |
| subjects affected / exposed          | 0 / 1 (0.00%) |  |  |
| occurrences (all)                    | 0             |  |  |
| Radiculopathy                        |               |  |  |
| subjects affected / exposed          | 0 / 1 (0.00%) |  |  |
| occurrences (all)                    | 0             |  |  |
| Syncope                              |               |  |  |
| subjects affected / exposed          | 0 / 1 (0.00%) |  |  |
| occurrences (all)                    | 0             |  |  |
| Somnolence                           |               |  |  |
| subjects affected / exposed          | 0 / 1 (0.00%) |  |  |
| occurrences (all)                    | 0             |  |  |
| Sciatica                             |               |  |  |
| subjects affected / exposed          | 0 / 1 (0.00%) |  |  |
| occurrences (all)                    | 0             |  |  |
| Taste disorder                       |               |  |  |
| subjects affected / exposed          | 0 / 1 (0.00%) |  |  |
| occurrences (all)                    | 0             |  |  |
| Blood and lymphatic system disorders |               |  |  |
| Anaemia                              |               |  |  |
| subjects affected / exposed          | 0 / 1 (0.00%) |  |  |
| occurrences (all)                    | 0             |  |  |
| Coagulopathy                         |               |  |  |
| subjects affected / exposed          | 0 / 1 (0.00%) |  |  |
| occurrences (all)                    | 0             |  |  |
| Eosinophilia                         |               |  |  |
| subjects affected / exposed          | 0 / 1 (0.00%) |  |  |
| occurrences (all)                    | 0             |  |  |

|   |                    |  |  |
|---|--------------------|--|--|
| Lymph node haemorrhage<br>subjects affected / exposed<br>occurrences (all)                        | 0 / 1 (0.00%)<br>0 |  |  |
| Lymph node pain<br>subjects affected / exposed<br>occurrences (all)                               | 0 / 1 (0.00%)<br>0 |  |  |
| Lymphadenopathy<br>subjects affected / exposed<br>occurrences (all)                               | 0 / 1 (0.00%)<br>0 |  |  |
| Neutropenia<br>subjects affected / exposed<br>occurrences (all)                                   | 0 / 1 (0.00%)<br>0 |  |  |
| Lymphopenia<br>subjects affected / exposed<br>occurrences (all)                                   | 0 / 1 (0.00%)<br>0 |  |  |
| Thrombocytopenia<br>subjects affected / exposed<br>occurrences (all)                              | 0 / 1 (0.00%)<br>0 |  |  |
| Ear and labyrinth disorders<br>Ear congestion<br>subjects affected / exposed<br>occurrences (all) | 0 / 1 (0.00%)<br>0 |  |  |
| Ear haemorrhage<br>subjects affected / exposed<br>occurrences (all)                               | 0 / 1 (0.00%)<br>0 |  |  |
| Ear pain<br>subjects affected / exposed<br>occurrences (all)                                      | 0 / 1 (0.00%)<br>0 |  |  |
| Vertigo<br>subjects affected / exposed<br>occurrences (all)                                       | 0 / 1 (0.00%)<br>0 |  |  |
| Eye disorders<br>Conjunctival haemorrhage<br>subjects affected / exposed<br>occurrences (all)     | 0 / 1 (0.00%)<br>0 |  |  |
| Dry eye   |                    |  |  |

|                             |                 |  |  |
|-----------------------------|-----------------|--|--|
| subjects affected / exposed | 0 / 1 (0.00%)   |  |  |
| occurrences (all)           | 0               |  |  |
| Vitreous haemorrhage        |                 |  |  |
| subjects affected / exposed | 0 / 1 (0.00%)   |  |  |
| occurrences (all)           | 0               |  |  |
| Vision blurred              |                 |  |  |
| subjects affected / exposed | 0 / 1 (0.00%)   |  |  |
| occurrences (all)           | 0               |  |  |
| Periorbital oedema          |                 |  |  |
| subjects affected / exposed | 0 / 1 (0.00%)   |  |  |
| occurrences (all)           | 0               |  |  |
| Gastrointestinal disorders  |                 |  |  |
| Abdominal pain upper        |                 |  |  |
| subjects affected / exposed | 0 / 1 (0.00%)   |  |  |
| occurrences (all)           | 0               |  |  |
| Abdominal pain              |                 |  |  |
| subjects affected / exposed | 1 / 1 (100.00%) |  |  |
| occurrences (all)           | 1               |  |  |
| Abdominal distension        |                 |  |  |
| subjects affected / exposed | 0 / 1 (0.00%)   |  |  |
| occurrences (all)           | 0               |  |  |
| Anal fissure                |                 |  |  |
| subjects affected / exposed | 0 / 1 (0.00%)   |  |  |
| occurrences (all)           | 0               |  |  |
| Anal haemorrhage            |                 |  |  |
| subjects affected / exposed | 0 / 1 (0.00%)   |  |  |
| occurrences (all)           | 0               |  |  |
| Aphthous ulcer              |                 |  |  |
| subjects affected / exposed | 0 / 1 (0.00%)   |  |  |
| occurrences (all)           | 0               |  |  |
| Angular cheilitis           |                 |  |  |
| subjects affected / exposed | 0 / 1 (0.00%)   |  |  |
| occurrences (all)           | 0               |  |  |
| Anal inflammation           |                 |  |  |
| subjects affected / exposed | 0 / 1 (0.00%)   |  |  |
| occurrences (all)           | 0               |  |  |

|                                  |                 |  |  |
|----------------------------------|-----------------|--|--|
| Ascites                          |                 |  |  |
| subjects affected / exposed      | 0 / 1 (0.00%)   |  |  |
| occurrences (all)                | 0               |  |  |
| Constipation                     |                 |  |  |
| subjects affected / exposed      | 0 / 1 (0.00%)   |  |  |
| occurrences (all)                | 0               |  |  |
| Diarrhoea                        |                 |  |  |
| subjects affected / exposed      | 0 / 1 (0.00%)   |  |  |
| occurrences (all)                | 0               |  |  |
| Dry mouth                        |                 |  |  |
| subjects affected / exposed      | 0 / 1 (0.00%)   |  |  |
| occurrences (all)                | 0               |  |  |
| Dyspepsia                        |                 |  |  |
| subjects affected / exposed      | 0 / 1 (0.00%)   |  |  |
| occurrences (all)                | 0               |  |  |
| Dysphagia                        |                 |  |  |
| subjects affected / exposed      | 1 / 1 (100.00%) |  |  |
| occurrences (all)                | 1               |  |  |
| Flatulence                       |                 |  |  |
| subjects affected / exposed      | 0 / 1 (0.00%)   |  |  |
| occurrences (all)                | 0               |  |  |
| Gastritis                        |                 |  |  |
| subjects affected / exposed      | 0 / 1 (0.00%)   |  |  |
| occurrences (all)                | 0               |  |  |
| Gastritis erosive                |                 |  |  |
| subjects affected / exposed      | 0 / 1 (0.00%)   |  |  |
| occurrences (all)                | 0               |  |  |
| Gastrointestinal disorder        |                 |  |  |
| subjects affected / exposed      | 0 / 1 (0.00%)   |  |  |
| occurrences (all)                | 0               |  |  |
| Gastrooesophageal reflux disease |                 |  |  |
| subjects affected / exposed      | 0 / 1 (0.00%)   |  |  |
| occurrences (all)                | 0               |  |  |
| Haemorrhoids                     |                 |  |  |
| subjects affected / exposed      | 0 / 1 (0.00%)   |  |  |
| occurrences (all)                | 0               |  |  |

|                                    |               |  |  |
|------------------------------------|---------------|--|--|
| Lip dry                            |               |  |  |
| subjects affected / exposed        | 0 / 1 (0.00%) |  |  |
| occurrences (all)                  | 0             |  |  |
| Melaena                            |               |  |  |
| subjects affected / exposed        | 0 / 1 (0.00%) |  |  |
| occurrences (all)                  | 0             |  |  |
| Lower gastrointestinal haemorrhage |               |  |  |
| subjects affected / exposed        | 0 / 1 (0.00%) |  |  |
| occurrences (all)                  | 0             |  |  |
| Nausea                             |               |  |  |
| subjects affected / exposed        | 0 / 1 (0.00%) |  |  |
| occurrences (all)                  | 0             |  |  |
| Odynophagia                        |               |  |  |
| subjects affected / exposed        | 0 / 1 (0.00%) |  |  |
| occurrences (all)                  | 0             |  |  |
| Oral mucosal erythema              |               |  |  |
| subjects affected / exposed        | 0 / 1 (0.00%) |  |  |
| occurrences (all)                  | 0             |  |  |
| Retching                           |               |  |  |
| subjects affected / exposed        | 0 / 1 (0.00%) |  |  |
| occurrences (all)                  | 0             |  |  |
| Stomatitis                         |               |  |  |
| subjects affected / exposed        | 0 / 1 (0.00%) |  |  |
| occurrences (all)                  | 0             |  |  |
| Subileus                           |               |  |  |
| subjects affected / exposed        | 0 / 1 (0.00%) |  |  |
| occurrences (all)                  | 0             |  |  |
| Toothache                          |               |  |  |
| subjects affected / exposed        | 0 / 1 (0.00%) |  |  |
| occurrences (all)                  | 0             |  |  |
| Vomiting                           |               |  |  |
| subjects affected / exposed        | 0 / 1 (0.00%) |  |  |
| occurrences (all)                  | 0             |  |  |
| Hepatobiliary disorders            |               |  |  |
| Cholangitis                        |               |  |  |

|  |               |  |  |
|--|---------------|--|--|
| subjects affected / exposed            | 0 / 1 (0.00%) |  |  |
| occurrences (all)                      | 0             |  |  |
| Hepatic cytolysis                      |               |  |  |
| subjects affected / exposed            | 0 / 1 (0.00%) |  |  |
| occurrences (all)                      | 0             |  |  |
| Hepatic pain                           |               |  |  |
| subjects affected / exposed            | 0 / 1 (0.00%) |  |  |
| occurrences (all)                      | 0             |  |  |
| Skin and subcutaneous tissue disorders |               |  |  |
| Dermatitis psoriasiform                |               |  |  |
| subjects affected / exposed            | 0 / 1 (0.00%) |  |  |
| occurrences (all)                      | 0             |  |  |
| Dermatitis acneiform                   |               |  |  |
| subjects affected / exposed            | 0 / 1 (0.00%) |  |  |
| occurrences (all)                      | 0             |  |  |
| Dry skin                               |               |  |  |
| subjects affected / exposed            | 0 / 1 (0.00%) |  |  |
| occurrences (all)                      | 0             |  |  |
| Intertrigo                             |               |  |  |
| subjects affected / exposed            | 0 / 1 (0.00%) |  |  |
| occurrences (all)                      | 0             |  |  |
| Macule                                 |               |  |  |
| subjects affected / exposed            | 0 / 1 (0.00%) |  |  |
| occurrences (all)                      | 0             |  |  |
| Night sweats                           |               |  |  |
| subjects affected / exposed            | 0 / 1 (0.00%) |  |  |
| occurrences (all)                      | 0             |  |  |
| Eczema                                 |               |  |  |
| subjects affected / exposed            | 0 / 1 (0.00%) |  |  |
| occurrences (all)                      | 0             |  |  |
| Erythema                               |               |  |  |
| subjects affected / exposed            | 0 / 1 (0.00%) |  |  |
| occurrences (all)                      | 0             |  |  |
| Prurigo                                |               |  |  |
| subjects affected / exposed            | 0 / 1 (0.00%) |  |  |
| occurrences (all)                      | 0             |  |  |



|                             |               |  |  |
|-----------------------------|---------------|--|--|
| Pruritus                    |               |  |  |
| subjects affected / exposed | 0 / 1 (0.00%) |  |  |
| occurrences (all)           | 0             |  |  |
| Psoriasis                   |               |  |  |
| subjects affected / exposed | 0 / 1 (0.00%) |  |  |
| occurrences (all)           | 0             |  |  |
| Petechiae                   |               |  |  |
| subjects affected / exposed | 0 / 1 (0.00%) |  |  |
| occurrences (all)           | 0             |  |  |
| Skin ulcer                  |               |  |  |
| subjects affected / exposed | 0 / 1 (0.00%) |  |  |
| occurrences (all)           | 0             |  |  |
| Rash                        |               |  |  |
| subjects affected / exposed | 0 / 1 (0.00%) |  |  |
| occurrences (all)           | 0             |  |  |
| Rash maculo-papular         |               |  |  |
| subjects affected / exposed | 0 / 1 (0.00%) |  |  |
| occurrences (all)           | 0             |  |  |
| Purpura                     |               |  |  |
| subjects affected / exposed | 0 / 1 (0.00%) |  |  |
| occurrences (all)           | 0             |  |  |
| Urticaria                   |               |  |  |
| subjects affected / exposed | 0 / 1 (0.00%) |  |  |
| occurrences (all)           | 0             |  |  |
| Renal and urinary disorders |               |  |  |
| Dysuria                     |               |  |  |
| subjects affected / exposed | 0 / 1 (0.00%) |  |  |
| occurrences (all)           | 0             |  |  |
| Haematuria                  |               |  |  |
| subjects affected / exposed | 0 / 1 (0.00%) |  |  |
| occurrences (all)           | 0             |  |  |
| Pollakiuria                 |               |  |  |
| subjects affected / exposed | 0 / 1 (0.00%) |  |  |
| occurrences (all)           | 0             |  |  |
| Urinary tract pain          |               |  |  |

|   |                    |  |  |
|---|--------------------|--|--|
| subjects affected / exposed<br>occurrences (all)  | 0 / 1 (0.00%)<br>0 |  |  |
| Urinary retention<br>subjects affected / exposed<br>occurrences (all)   | 0 / 1 (0.00%)<br>0 |  |  |
| Renal failure<br>subjects affected / exposed<br>occurrences (all)   | 0 / 1 (0.00%)<br>0 |  |  |
| Endocrine disorders<br>Hyperthyroidism<br>subjects affected / exposed<br>occurrences (all)                        | 0 / 1 (0.00%)<br>0 |  |  |
| Musculoskeletal and connective tissue disorders<br>Arthralgia<br>subjects affected / exposed<br>occurrences (all) | 0 / 1 (0.00%)<br>0 |  |  |
| Back pain<br>subjects affected / exposed<br>occurrences (all)   | 0 / 1 (0.00%)<br>0 |  |  |
| Bone pain<br>subjects affected / exposed<br>occurrences (all)   | 0 / 1 (0.00%)<br>0 |  |  |
| Flank pain<br>subjects affected / exposed<br>occurrences (all)  | 0 / 1 (0.00%)<br>0 |  |  |
| Groin pain<br>subjects affected / exposed<br>occurrences (all)  | 0 / 1 (0.00%)<br>0 |  |  |
| Muscular weakness<br>subjects affected / exposed<br>occurrences (all)   | 0 / 1 (0.00%)<br>0 |  |  |
| Muscle spasms<br>subjects affected / exposed<br>occurrences (all)   | 0 / 1 (0.00%)<br>0 |  |  |
| Myalgia   |                    |  |  |

|                               |               |  |  |
|-------------------------------|---------------|--|--|
| subjects affected / exposed   | 0 / 1 (0.00%) |  |  |
| occurrences (all)             | 0             |  |  |
| Neck pain                     |               |  |  |
| subjects affected / exposed   | 0 / 1 (0.00%) |  |  |
| occurrences (all)             | 0             |  |  |
| Pain in extremity             |               |  |  |
| subjects affected / exposed   | 0 / 1 (0.00%) |  |  |
| occurrences (all)             | 0             |  |  |
| Pubic pain                    |               |  |  |
| subjects affected / exposed   | 0 / 1 (0.00%) |  |  |
| occurrences (all)             | 0             |  |  |
| Infections and infestations   |               |  |  |
| Bronchitis                    |               |  |  |
| subjects affected / exposed   | 0 / 1 (0.00%) |  |  |
| occurrences (all)             | 0             |  |  |
| Bronchitis viral              |               |  |  |
| subjects affected / exposed   | 0 / 1 (0.00%) |  |  |
| occurrences (all)             | 0             |  |  |
| Clostridial infection         |               |  |  |
| subjects affected / exposed   | 0 / 1 (0.00%) |  |  |
| occurrences (all)             | 0             |  |  |
| Clostridium difficile colitis |               |  |  |
| subjects affected / exposed   | 0 / 1 (0.00%) |  |  |
| occurrences (all)             | 0             |  |  |
| Conjunctivitis                |               |  |  |
| subjects affected / exposed   | 0 / 1 (0.00%) |  |  |
| occurrences (all)             | 0             |  |  |
| Erysipelas                    |               |  |  |
| subjects affected / exposed   | 0 / 1 (0.00%) |  |  |
| occurrences (all)             | 0             |  |  |
| Diverticulitis                |               |  |  |
| subjects affected / exposed   | 0 / 1 (0.00%) |  |  |
| occurrences (all)             | 0             |  |  |
| Cystitis                      |               |  |  |
| subjects affected / exposed   | 0 / 1 (0.00%) |  |  |
| occurrences (all)             | 0             |  |  |

|                                     |               |  |  |
|-------------------------------------|---------------|--|--|
| Gastroenteritis                     |               |  |  |
| subjects affected / exposed         | 0 / 1 (0.00%) |  |  |
| occurrences (all)                   | 0             |  |  |
| Folliculitis                        |               |  |  |
| subjects affected / exposed         | 0 / 1 (0.00%) |  |  |
| occurrences (all)                   | 0             |  |  |
| Escherichia urinary tract infection |               |  |  |
| subjects affected / exposed         | 0 / 1 (0.00%) |  |  |
| occurrences (all)                   | 0             |  |  |
| Genital herpes simplex              |               |  |  |
| subjects affected / exposed         | 0 / 1 (0.00%) |  |  |
| occurrences (all)                   | 0             |  |  |
| Genital infection fungal            |               |  |  |
| subjects affected / exposed         | 0 / 1 (0.00%) |  |  |
| occurrences (all)                   | 0             |  |  |
| Herpes dermatitis                   |               |  |  |
| subjects affected / exposed         | 0 / 1 (0.00%) |  |  |
| occurrences (all)                   | 0             |  |  |
| Impetigo                            |               |  |  |
| subjects affected / exposed         | 0 / 1 (0.00%) |  |  |
| occurrences (all)                   | 0             |  |  |
| Herpes zoster                       |               |  |  |
| subjects affected / exposed         | 0 / 1 (0.00%) |  |  |
| occurrences (all)                   | 0             |  |  |
| Influenza                           |               |  |  |
| subjects affected / exposed         | 0 / 1 (0.00%) |  |  |
| occurrences (all)                   | 0             |  |  |
| Infection                           |               |  |  |
| subjects affected / exposed         | 0 / 1 (0.00%) |  |  |
| occurrences (all)                   | 0             |  |  |
| Nasopharyngitis                     |               |  |  |
| subjects affected / exposed         | 0 / 1 (0.00%) |  |  |
| occurrences (all)                   | 0             |  |  |
| Oesophageal infection               |               |  |  |
| subjects affected / exposed         | 0 / 1 (0.00%) |  |  |
| occurrences (all)                   | 0             |  |  |

|                                       |               |  |  |
|---------------------------------------|---------------|--|--|
| Pharyngitis                           |               |  |  |
| subjects affected / exposed           | 0 / 1 (0.00%) |  |  |
| occurrences (all)                     | 0             |  |  |
| Oral herpes                           |               |  |  |
| subjects affected / exposed           | 0 / 1 (0.00%) |  |  |
| occurrences (all)                     | 0             |  |  |
| Pneumonia                             |               |  |  |
| subjects affected / exposed           | 0 / 1 (0.00%) |  |  |
| occurrences (all)                     | 0             |  |  |
| Rash pustular                         |               |  |  |
| subjects affected / exposed           | 0 / 1 (0.00%) |  |  |
| occurrences (all)                     | 0             |  |  |
| Respiratory tract infection           |               |  |  |
| subjects affected / exposed           | 0 / 1 (0.00%) |  |  |
| occurrences (all)                     | 0             |  |  |
| Respiratory tract infection bacterial |               |  |  |
| subjects affected / exposed           | 0 / 1 (0.00%) |  |  |
| occurrences (all)                     | 0             |  |  |
| Sinusitis                             |               |  |  |
| subjects affected / exposed           | 0 / 1 (0.00%) |  |  |
| occurrences (all)                     | 0             |  |  |
| Tooth abscess                         |               |  |  |
| subjects affected / exposed           | 0 / 1 (0.00%) |  |  |
| occurrences (all)                     | 0             |  |  |
| Tooth infection                       |               |  |  |
| subjects affected / exposed           | 0 / 1 (0.00%) |  |  |
| occurrences (all)                     | 0             |  |  |
| Tracheitis                            |               |  |  |
| subjects affected / exposed           | 0 / 1 (0.00%) |  |  |
| occurrences (all)                     | 0             |  |  |
| Upper respiratory tract infection     |               |  |  |
| subjects affected / exposed           | 0 / 1 (0.00%) |  |  |
| occurrences (all)                     | 0             |  |  |
| Urinary tract infection enterococcal  |               |  |  |
| subjects affected / exposed           | 0 / 1 (0.00%) |  |  |
| occurrences (all)                     | 0             |  |  |

|                                    |                 |  |  |
|------------------------------------|-----------------|--|--|
| Urinary tract infection            |                 |  |  |
| subjects affected / exposed        | 0 / 1 (0.00%)   |  |  |
| occurrences (all)                  | 0               |  |  |
| Mucosal infection                  |                 |  |  |
| subjects affected / exposed        | 1 / 1 (100.00%) |  |  |
| occurrences (all)                  | 1               |  |  |
| Stoma site infection               |                 |  |  |
| subjects affected / exposed        | 1 / 1 (100.00%) |  |  |
| occurrences (all)                  | 1               |  |  |
| Metabolism and nutrition disorders |                 |  |  |
| Acidosis                           |                 |  |  |
| subjects affected / exposed        | 0 / 1 (0.00%)   |  |  |
| occurrences (all)                  | 0               |  |  |
| Decreased appetite                 |                 |  |  |
| subjects affected / exposed        | 0 / 1 (0.00%)   |  |  |
| occurrences (all)                  | 0               |  |  |
| Cell death                         |                 |  |  |
| subjects affected / exposed        | 0 / 1 (0.00%)   |  |  |
| occurrences (all)                  | 0               |  |  |
| Dehydration                        |                 |  |  |
| subjects affected / exposed        | 0 / 1 (0.00%)   |  |  |
| occurrences (all)                  | 0               |  |  |
| Fluid retention                    |                 |  |  |
| subjects affected / exposed        | 0 / 1 (0.00%)   |  |  |
| occurrences (all)                  | 0               |  |  |
| Folate deficiency                  |                 |  |  |
| subjects affected / exposed        | 0 / 1 (0.00%)   |  |  |
| occurrences (all)                  | 0               |  |  |
| Gout                               |                 |  |  |
| subjects affected / exposed        | 0 / 1 (0.00%)   |  |  |
| occurrences (all)                  | 0               |  |  |
| Hypercalcaemia                     |                 |  |  |
| subjects affected / exposed        | 0 / 1 (0.00%)   |  |  |
| occurrences (all)                  | 0               |  |  |
| Hyperkalaemia                      |                 |  |  |

|                             |               |  |  |
|-----------------------------|---------------|--|--|
| subjects affected / exposed | 0 / 1 (0.00%) |  |  |
| occurrences (all)           | 0             |  |  |
| Hyperglycaemia              |               |  |  |
| subjects affected / exposed | 0 / 1 (0.00%) |  |  |
| occurrences (all)           | 0             |  |  |
| Hyperphosphataemia          |               |  |  |
| subjects affected / exposed | 0 / 1 (0.00%) |  |  |
| occurrences (all)           | 0             |  |  |
| Hypoalbuminaemia            |               |  |  |
| subjects affected / exposed | 0 / 1 (0.00%) |  |  |
| occurrences (all)           | 0             |  |  |
| Hypocalcaemia               |               |  |  |
| subjects affected / exposed | 0 / 1 (0.00%) |  |  |
| occurrences (all)           | 0             |  |  |
| Hypokalaemia                |               |  |  |
| subjects affected / exposed | 0 / 1 (0.00%) |  |  |
| occurrences (all)           | 0             |  |  |
| Hypomagnesaemia             |               |  |  |
| subjects affected / exposed | 0 / 1 (0.00%) |  |  |
| occurrences (all)           | 0             |  |  |
| Hyponatraemia               |               |  |  |
| subjects affected / exposed | 0 / 1 (0.00%) |  |  |
| occurrences (all)           | 0             |  |  |
| Hypophosphataemia           |               |  |  |
| subjects affected / exposed | 0 / 1 (0.00%) |  |  |
| occurrences (all)           | 0             |  |  |
| Malnutrition                |               |  |  |
| subjects affected / exposed | 0 / 1 (0.00%) |  |  |
| occurrences (all)           | 0             |  |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date              | Amendment   |
|-------------------|---|
| 02 September 2015 | 1st global protocol amendment: The potential Cytochrome P450 (CYP) inducing effect was addressed in the amended Clinical Trial Protocol (CTP) and a non-exhaustive list of CYP 3A4, 2C8 and 1A2 substrates was added (Section 10.6 of the CTP). Furthermore, it was added to inclusion criterion 6 that an additional barrier method is necessary for women of childbearing potential using a contraceptive pill due to the potential CYP3A4 inducing effect of BI 894999.  |
| 08 April 2016     | 2nd global protocol amendment: A second dosing schedule (Schedule B: 3-week cycles [21 days] with 2 weeks on treatment and 1 week off treatment) was introduced. The evaluation of BI 894999 (Schedule A: continuous dosing in 3-week cycles) in patients with Non-Hodgkin Lymphoma (NHL) was initiated. The secondary pharmacokinetics (PK) endpoints were reduced, and some secondary PK parameters were re-defined as further endpoints.   |
| 23 November 2016  | 3rd global protocol amendment: Precautionary measures were introduced because of cardiac findings in patients participating in the trial. The measures were applicable to all ongoing patients who had benefited from the treatment in order to allow them to continue the treatment under close cardiac safety monitoring. Further enrolment into the trial was stopped.   |
| 12 May 2017       | 4th global protocol amendment: External cardiologists concluded that the cause of the troponin elevation was unclear. Patients could continue on treatment with appropriate monitoring. Cardiac monitoring was adapted. Patients in the NHL cohort were to be treated with the Schedule selected by the Data Monitoring Committee (DMC) once Maximum Tolerated dose (MTD) had been determined for both Schedules A and B in patients with solid tumours. The Dose Limiting Toxicity (DLT) definition was revised. |
| 18 October 2017   | 5th global protocol amendment: Changes were introduced to restrict the definition of NHL to allow analyses of results in a more homogenous population. The NHL cohort was restricted to DLBCL patients. The protocol was amended to reflect the selection of 4 types of solid tumours (SCLC, mCRPC, CRC and NC) to be tested in the Phase 1b part of the study.   |
| 25 June 2018      | 6th global protocol amendment: The protocol was revised to clarify the significance of drug-related troponin Common Terminology Criteria for Adverse Events (CTCAE) grade 3.  |
| 05 September 2018 | 7th global protocol amendment: NC allowed inclusion of minor patients (aged $\geq 15$ years at the time of consent). The NC cohort was also extended to up to 20 patients. NC patients who were progressing under trial treatment could continue with treatment if they derived clinical benefit and no other treatment option was available.   |
| 05 November 2018  | 8th global protocol amendment: Included clarifications and changes for consistency that were introduced following review of protocol version 7.0 by the Bundesinstitut für Arzneimittel und Medizinprodukte (BfArM) authority in Germany and of protocol version 8.0 by the U.S. Food and Drug Administration (US FDA).   |
| 05 February 2019  | 9th global protocol amendment: A third intermittent dose escalation was added (Schedule C) in Phase Ia.   |



|                   |   |
|-------------------|---|
| 24 September 2019 | 10th global protocol amendment: If Schedule C appeared to have a better tolerability in patients with solid tumours than Schedule B, this could be extended to NC patients. Overall survival was added as an endpoint for patients with NC. Time to treatment failure was also added as an endpoint. Eligibility criteria were revised for including patients with NC due to their likely fast progression and the lack of any other treatment options in this indication. NC patients who had a mixed radiological response to treatment could remain on treatment if they derived clinical benefit. |
| 24 June 2020      | 11th global protocol amendment: Due to the COVID-19 pandemic, the protocol was adapted to minimise in-patient visits.   |

Notes:

## Interruptions (globally)

Were there any global interruptions to the trial? Yes

| Date            | Interruption   | Restart date  |
|-----------------|--|---------------|
| 04 October 2016 | On 04 Oct 2016, the sponsor decided to put a temporary hold on further recruitment of patients in trial 1367.1. The measure was taken since review of patient data revealed some patients with increased troponin levels. A thorough review by cardiologists was initiated with regards to troponin levels, Electrocardiogram (ECG), and clinical summaries of all enrolled patients. Evidence supporting a causal association between the increased laboratory troponin values and the administration of the trial medication could not be established. There were no corresponding clinically significant findings based on the reviewed ECGs and the clinical summaries of enrolled patients. The external review concluded that the cause of troponin elevation may be multifactorial in the trial patient population. In conclusion, the findings were considered to not preclude further clinical development. Consequently, patient recruitment was re-started on 25-April-2017. Ongoing patients continued the treatment during the time that recruitment was put on hold. | 25 April 2017 |

Notes:

## Limitations and caveats

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

This trial was closed in accordance with protocol-defined criteria for stopping the trial following assessments of futility. Trial was completed as described in protocol.

Notes: